News Release

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Merck KGaA, Darmstadt, Germany Announces Update on the INTR@PID Clinical Program Including Lung 037 Study

Darmstadt, Germany, January 20, 2021 – Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced an update on the Phase III INTR@PID Lung 037 study and the extensive INTR@PID clinical trial program for the potential first-in-class investigational bifunctional immunotherapy bintrafusp alfa, in difficult-to-treat cancers, including biliary tract cancer (BTC) and cervical cancer.

The comprehensive INTR@PID program is designed to assess the impact of bintrafusp alfa across distinct cancers and settings where TGF-β is thought to play a driving role. TGF-β is a cytokine that is known to be associated with tumor propagation and metastatic potential such as local immunosuppression, fibrosis, growth of tumor blood vessels and chemo- or radiotherapy resistance through several mechanisms. Trapping TGF-β in the tumor microenvironment on top of PD-L1 blockade is thought to be transformative in different clinical settings.

While reviewing the totality of data from the ongoing clinical trial INTR@PID Lung 037 in the first-line treatment of patients with stage IV non-small cell lung cancer (NSCLC) that have high expression of PD-L1, the Independent Data Monitoring Committee recommended on January 19, 2021 to discontinue the clinical trial. Based on this recommendation, Merck KGaA, Darmstadt, Germany has made the

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decision to discontinue the clinical trial, as the study is unlikely to meet the co-primary endpoint, specifically progression-free survival. The recommendation by the Independent Data Monitoring Committee and the Company's decision is related only to this clinical trial.

"We have pioneered the science behind bintrafusp alfa, and now through a strategic alliance, multiple non-correlated parallel hypotheses are being evaluated across numerous indications in our extensive INTR@PID clinical program," said Danny Bar-Zohar, M.D., Global Head of Development for the Healthcare business of Merck KGaA, Darmstadt, Germany. "We remain committed to further evaluation of bintrafusp alfa, and these data from INTR@PID Lung 037 will provide important insights that may be applied to future studies."

Ongoing and New Clinical Trials

- BTC: Topline results for the INTR@PID BTC 047 study are planned for Q1. Additionally, a Phase II/III study of bintrafusp alfa in combination with chemotherapy as a first-line treatment for BTC (INTR@PID BTC 055), which is assessing a different hypothesis than the second-line monotherapy study, has completed enrollment in the Phase II portion and is on track for the Phase III portion. In 2020, the Japan Ministry of Health, Labour and Welfare granted SAKIGAKE 'fast-track' designation for bintrafusp alfa in BTC, a regulatory designation that enables an expedited review and is connected to indications with limited standards of care.

- Cervical Cancer: The Phase II cervical cancer study (INTR@PID CERVICAL 017) initiated in 2020 is currently ongoing with enrollment nearing completion. The study is evaluating bintrafusp alfa for the treatment of patients with advanced, unresectable cervical cancer that progressed during or after platinum-containing chemotherapy. Human papillomavirus (HPV) infection has been closely associated with increased TGF-β expression in a variety of solid tumors, including cervical cancer.[1] Encouraging efficacy of bintrafusp alfa in HPV-associated malignancies was reported from a pooled analysis of the Phase I (INTR@PID SOLID TUMOR 001) and a Phase II NCI-led trial.[2] A new Phase I study in locally

advanced/advanced cervical cancer as a combination therapy (INTR@PID CERVICAL 046) was also initiated in 2020.

- NSCLC: The bintrafusp alfa lung program is designed to assess the patient population that may benefit from the dual mechanism of action focusing on combination studies (INTR@PID LUNG 005, INTR@PID LUNG 024). In addition to studying combinations with standards of care, the INTR@PID LUNG 024 study will expand to include new combinations, including combining with VEGF inhibitors, CTLA-4 targeted immunotherapies, and PARP inhibitors.

- New Studies: Recently initiated monotherapy studies include a Phase II monotherapy study in patients with triple-negative breast cancer expressing high mobility group AT-hook 2 (HMGA2) (INTR@PID BREAST 020) and a Phase I monotherapy study in locally advanced/metastatic urothelial cancer (INTR@PID UROTHELIAL 152). A new Phase I multi-arm platform study combining bintrafusp alfa with GSK's iCOS (feladilimab) is initiating.

**Bintrafusp alfa is currently under clinical investigation and not approved for any use anywhere in the world.*

About Biliary Tract Cancer (BTC)
BTCs are a group of rare, aggressive gastrointestinal cancers associated with poor outcomes and limited treatment options. There is currently no globally accepted standard of care in the second-line setting and chemotherapy as well as immunotherapies have demonstrated low response rates in BTC. Epithelial-to-mesenchymal transition (EMT), a hallmark of tumor progression and drug resistance, plays an important role in BTC and has been shown to be triggered by TGF-β signaling.

About Cervical Cancer
The human papillomavirus (HPV) is responsible for more than 90 percent of cervical cancer cases and is one of the most common and deadliest cancers among women worldwide. The TGF-β pathway is frequently dysregulated in HPV-associated malignancies, including cervical cancer, and may contribute to development and progression of cervical cancer and generating resistance to immunotherapy. There is no globally accepted standard-of-care treatment for recurrent/metastatic cervical cancer after first-line systemic therapy.

About Non-small Cell Lung Cancer (NSCLC)
Non-small cell lung cancer remains one of the leading causes of cancer deaths worldwide with low five-year survival rates. There has been significant treatment progress with checkpoint inhibitors, but a majority of patients don't respond.

About Bintrafusp Alfa
Bintrafusp alfa (M7824), discovered in-house at Merck KGaA, Darmstadt, Germany, and currently in clinical development through a strategic alliance with GSK, is a potential first-in-class investigational bifunctional fusion protein designed to simultaneously block two immunosuppressive pathways, TGF-β and PD-L1, within the tumor microenvironment. This bifunctional approach is thought to control tumor growth by potentially restoring and enhancing anti-tumor responses. In preclinical studies, bintrafusp alfa has demonstrated antitumor activity both as monotherapy and in combination with chemotherapy. Based on its mechanism of action, bintrafusp alfa offers a potential targeted approach to addressing the underlying pathophysiology of difficult-to-treat cancers.

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About the INTR@PID Clinical Trial Program
INTR@PID is a global clinical trial program investigating the potential co-localized, dual inhibition of TGF-β and PD-L1 with bintrafusp alfa (M7824) in multiple tumor types. Current clinical trial information can be found on the INTR@PID website at www.intrapidclinicaltrials.com. To date, more than 1,300 patients with various types of solid tumors have been treated globally in the bintrafusp alfa INTR@PID clinical development program.

The INTR@PID clinical development strategy is comprehensive and is pursuing non-redundant hypotheses grounded in preclinical and early clinical data findings that continue to be explored and may yield clinically meaningful insights to patients in need, including exploring settings where simultaneous, synchronized targeting of TGF-β and PD-L1 may offer the key to expanding the potential of immunotherapy (lung cancer program); focusing on opportunities where PD-1/PD-L1 has suboptimal clinical activities and pathogenesis linked to TGF-β biology (studies in BTC and in urothelial cancers); and targeting specific tumors with biomarkers with a strong link to TGF-β signaling pathway (studies in TNBC and cervical cancer).

About Merck KGaA, Darmstadt, Germany
Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across healthcare, life science and performance materials. Around 58,000 employees work to make a positive difference to millions of people's lives every day by creating more joyful and sustainable ways to live. From advancing gene editing technologies and discovering unique ways to treat the most challenging diseases to enabling the intelligence of devices – the company is everywhere. In 2019, Merck KGaA, Darmstadt, Germany, generated sales of € 16.2 billion in 66 countries.

The company holds the global rights to the name and trademark "Merck" internationally. The only exceptions are the United States and Canada, where the business sectors of Merck KGaA, Darmstadt, Germany, operate as EMD Serono in healthcare, MilliporeSigma in life science, and EMD Performance Materials. Since its founding in 1668, scientific exploration and responsible entrepreneurship have been key to the company's technological and scientific advances. To this day, the founding family remains the majority owner of the publicly listed company.

References
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2. Strauss J, Gatti-Mays ME, Cho BC, et al. Bintrafusp alfa, a bifunctional fusion protein targeting TGF-β and PD-L1, in patients with human papillomavirus-associated malignancies. J Immunother Cancer. 2020;8:e001395.