

## News Release

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## **Merck KGaA, Darmstadt, Germany, Reports Topline Data for Bintrafusp Alfa as Second-Line Monotherapy Treatment in Biliary Tract Cancer**

Darmstadt, Germany, March 16, 2021– Merck KGaA, Darmstadt, Germany, a leading science and technology company, today announced topline data from the Phase II INTR@PID BTC 047 study evaluating bintrafusp alfa as a monotherapy in the second-line treatment of patients with locally advanced or metastatic biliary tract cancer (BTC) who have failed or are intolerant of first-line platinum-based chemotherapy.

In the study of 159 patients, bintrafusp alfa demonstrated single-agent efficacy and durability with a manageable safety profile after more than nine months of follow-up, with an Independent Review Committee (IRC)-adjudicated objective response rate (ORR) of 10.1% (95% CI: 5.9% to 15.8%) per RECIST 1.1. Though single-agent activity was observed, the study did not meet the pre-defined threshold that would have enabled regulatory filing for BTC in the second line setting. The results will be submitted for presentation at an upcoming medical meeting or publication.

“Given the high unmet treatment need in BTC, where single agent immunotherapy in PD-L1 all comers has shown an ORR of 5.8%, we are encouraged by the single agent clinical activity of bintrafusp alfa in this study as a second-line treatment,” said Milind Javle, MD, professor of GI medical oncology, MD Anderson Cancer Center, and an investigator for the INTR@PID BTC 047 study. “The bintrafusp alfa

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047 study is one of the most important clinical investigations conducted for chemo-refractory biliary cancers, and I would like to thank the patients, families, and study team for their valuable participation.”

“This study demonstrates single-agent activity with bintrafusp alfa in locally advanced or metastatic BTC, a disease that has been historically difficult to treat,” said Danny Bar-Zohar, M.D., Global Head of Development for the Healthcare business sector of Merck KGaA, Darmstadt, Germany. “The data will contribute to our understanding of addressing both TGF- $\beta$  and PD-L1 inhibition in the tumor microenvironment.”

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 currently ongoing.

*\*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- $\beta$  signaling.

### **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- $\beta$  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.

### **About the INTR@PID Clinical Trial Program**

INTR@PID is a global clinical trial program investigating the potential co-localized, dual inhibition of TGF- $\beta$  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](http://www.intrapidclinicaltrials.com). To date, globally more than 1,300 patients with various types of solid tumors have received bintrafusp alfa in the 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- $\beta$  and PD-L1 may offer the key to expanding the potential of immunotherapy; focusing on opportunities where PD-1/PD-L1 has suboptimal clinical activities and pathogenesis linked to TGF- $\beta$  biology; and targeting specific tumors with biomarkers with a strong link to TGF- $\beta$  signaling pathway.

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### **About Merck KGaA, Darmstadt, Germany**

Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across healthcare, life science and electronics. 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 2020, Merck KGaA, Darmstadt, Germany, generated sales of € 17.5 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 Electronics. 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.