

**ONO PHARMACEUTICAL CO., LTD.**

**Bristol-Myers Squibb Company**

**Kyowa Hakko Kirin Co., Ltd.**

**ONO PHARMACEUTICAL, Bristol-Myers Squibb and Kyowa Hakko Kirin Announce  
Immuno-Oncology Clinical Collaboration Studying  
*Opdivo* (nivolumab) and Mogamulizumab in Advanced Solid Tumors**

(OSAKA, NEW YORK and TOKYO– December 10, 2014) - ONO PHARMACEUTICAL CO., LTD. (Tokyo: 4528 “ONO”), Bristol-Myers Squibb Company (NYSE: BMY) and Kyowa Hakko Kirin Co., Ltd. (Tokyo: 4151, “Kyowa Hakko Kirin” ) announced today the companies have entered into a clinical trial collaboration agreement to conduct a Phase 1 combination study with *Opdivo* (nivolumab), a PD-1 immune checkpoint inhibitor, and mogamulizumab, an anti-CCR4 antibody. The study, which will be conducted in Japan, will focus on evaluating the safety, tolerability and anti-tumor activity of combining *Opdivo* and mogamulizumab as a potential treatment option for patients with advanced or metastatic solid tumors.

*Opdivo*, launched in Japan in September 2014 for the treatment of patients with unresectable melanoma, is being developed in multiple tumor types in more than 50 clinical trials worldwide. Mogamulizumab was launched in Japan in May 2012 for the treatment of relapsed or refractory CCR4-positive Adult T-cell Leukemia-Lymphoma (ATL), and granted the indication expansion in March 2014 for relapsed or refractory CCR4-positive Peripheral T-Cell Lymphoma (PTCL) and Cutaneous T-Cell Lymphoma (CTCL). Clinical trials with mogamulizumab in ATL, PTCL, and CTCL are ongoing in the US, EU and other countries.

*Opdivo* and mogamulizumab are part of a new class of cancer treatments known as immunotherapies, which are designed to harness the body’s own immune system in fighting cancer by targeting distinct regulatory components of the immune system. *Opdivo* binds to the checkpoint receptor PD-1 expressed on activated T-cells, blocking this pathway and enabling the immune system to attack tumors, while mogamulizumab can suppress some of the immune cells that shield the tumor from the immune system. Pre-clinical evidence for each therapy suggests the combination of *Opdivo* and mogamulizumab may lead to an enhanced anti-tumor immune response compared to either agent alone.

“Studying combination regimens of immunotherapies offers the opportunity to explore the potential of enhanced efficacy compared to current standards of care in treating cancer,” said Hiroshi Awata, Member of the Board of Directors, Vice President Executive Officer/ Executive Director, Clinical Development & Clinical Development Planning, ONO. “We are delighted to be able to

pursue the possibility of immunotherapies through this collaboration with Kyowa Hakko Kirin. We believe that there is a strong rationale to explore the combination of *Opdivo* and mogamulizumab with the goal of identifying a new treatment option for these cancer patients.”

“Our collaboration with Kyowa Hakko Kirin further complements the broad clinical development program for *Opdivo*, will advance our understanding of the combination of *Opdivo* and mogamulizumab, and is an example of our commitment to develop combination immuno-oncology regimens for patients with metastatic cancer,” stated Michael Giordano, senior vice president, Head of Development, Oncology, Bristol-Myers Squibb.

“It is exciting for us to build a partnership with ONO and BMS in immuno-oncology,” said Yoichi Sato, Managing Executive Officer, Vice President, Head of Research and Development Division of Kyowa Hakko Kirin. “The planned combination study will help determine whether the combination of these two immunotherapies can deliver better outcomes in patients with advanced cancers.”

The study will be conducted by ONO and Kyowa Hakko Kirin. Additional details of the collaboration were not disclosed.

### **About *Opdivo* (nivolumab)**

Cancer cells may exploit “regulatory” pathways, such as checkpoint pathways, to hide from the immune system and shield the tumor from immune attack. *Opdivo* is an investigational, human PD-1 immune checkpoint inhibitor that binds to the checkpoint receptor PD-1 expressed on activated T-cells.

*Opdivo* is being studied across multiple tumor types in more than 50 trials – as monotherapy or in combination with other therapies – in which more than 7,000 patients have been enrolled worldwide. Among these are several potentially registrational trials in NSCLC, melanoma, renal cell carcinoma (RCC), head and neck cancer, glioblastoma and non-Hodgkin lymphoma (NHL).

In 2012, the FDA granted Fast Track designation for *Opdivo* in NSCLC, melanoma and RCC. In April 2014, the company initiated a rolling submission with the FDA for *Opdivo* in third-line pre-treated squamous cell NSCLC and expects to complete the submission by year-end. The FDA granted *Opdivo* Breakthrough Therapy Designation in May 2014 for the treatment of patients with Hodgkin lymphoma after failure of autologous stem cell transplant and brentuximab. On July 4, ONO PHARMACEUTICAL CO. announced that *Opdivo* received manufacturing and marketing approval in Japan for the treatment of patients with unresectable melanoma and launched on September 2, making *Opdivo* the first PD-1 immune checkpoint inhibitor approved and launched anywhere in the

world. On September 26, Bristol-Myers Squibb announced that the FDA accepted for priority review the Biologics License Application for previously treated advanced melanoma, and the Prescription Drug User Fee Act goal date for a decision is March 30, 2015. The FDA also granted *Opdivo* Breakthrough Therapy status for this indication. In the European Union, the European Medicines Agency (EMA) has validated for review the Marketing Authorization Application (MAA) for *Opdivo* in advanced melanoma. The application has also been granted accelerated assessment by the EMA's Committee for Medicinal Products for Human Use. The EMA also validated for review the MAA for *Opdivo* in NSCLC.

### **About Mogamulizumab**

Mogamulizumab (Brand name: POTELOGE<sup>®</sup>) is a novel, humanized mAb directed against CC chemokine receptor type 4 (CCR4). Engineered by Kyowa Hakko Kirin's unique POTELOGENT<sup>®</sup> Technology, the antibody is designed to kill its target cells through potent antibody-dependent cellular cytotoxicity. Mogamulizumab was launched in Japan in May 2012 for the treatment of patients with relapsed or refractory CCR4-positive adult T-cell leukemia-lymphoma (ATL). The drug was approved for indication expansion and was granted marketing authorization in Japan for the treatment of patients with relapsed or refractory CCR4-positive, peripheral T-cell lymphoma (PTCL) and cutaneous T-cell lymphoma (CTCL) in March 2014. Clinical trials with mogamulizumab in ATL, PTCL, and CTCL are ongoing in the US, EU and other countries.

### **About ONO**

ONO PHARMACEUTICAL, headquartered in Osaka, Japan, is an R&D-oriented pharmaceutical company committed to creating innovative medicines in specific areas. It focuses especially on the diabetes and oncology areas. For more information, please visit the company's website at <http://www.ono.co.jp/eng/index.html>.

### **About Bristol-Myers Squibb**

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information, please visit [www.bms.com](http://www.bms.com) or follow us on Twitter at <http://twitter.com/bmsnews>.

### **About the Bristol-Myers Squibb and ONO PHARMACEUTICAL Collaboration**

In 2011, through a collaboration agreement with ONO PHARMACEUTICAL CO., Bristol-Myers Squibb expanded its territorial rights to develop and commercialize *Opdivo* globally except in Japan, South Korea and Taiwan, where ONO had retained all rights to the compound at the time. On

July 23, 2014, Bristol-Myers Squibb and ONO further expanded the companies' strategic collaboration agreement to jointly develop and commercialize multiple immunotherapies – as single agents and combination regimens – for patients with cancer in Japan, South Korea and Taiwan.

### **About Kyowa Hakko Kirin**

Kyowa Hakko Kirin is a leading biopharmaceutical company in Japan focusing on its core business area of oncology, nephrology and immunology/allergy. Kyowa Hakko Kirin leverages antibody-related leading-edge technologies to discover and develop innovative new drugs aiming to become a global specialty pharmaceutical company which contributes to the health and well-being of people around the world. For more information, visit <http://www.kyowa-kirin.com>.

### **Bristol-Myers Squibb Forward-Looking Statement**

*This press release contains “forward-looking statements” as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding the research, development and commercialization of pharmaceutical products. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among other risks, there can be no guarantee that this combination regimen will receive regulatory approval, or, if approved, that it will become a commercially successful product. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2013 in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.*

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