PRESS RELEASE

June 1, 2016
TMRC Co., Ltd

FDA Accepts IND to Advance TM-411 submitted as SY-1425 by Syros into Phase 2 Clinical Trial in Acute Myeloid Leukemia (AML) and Myelodysplastic Syndrome (MDS)

The U.S. Food and Drug Administration (FDA) accepted the Investigational New Drug (IND) application to advance SY-1425 (TM-411, tamibarotene) into a Phase 2 clinical trial in genomically defined subsets of patients with relapsed or refractory acute myeloid leukemia (AML) and relapsed high-risk myelodysplastic syndrome (MDS) identified through Syros Pharmaceuticals Inc.'s platform.

TMRC Co., Ltd. ("TMRC" Hisao Ekimoto, President & CEO, Tokyo, Japan) entered into an exclusive license agreement with Syros Pharmaceuticals ("Syros" Nancy Simonian, CEO, Massachusetts, USA) to develop and commercialize TM-411 in North America and Europe for cancer on September 11, 2015. Syros has been preparing to enter the clinical trial thereafter and recently submitted the IND on TM-411 as SY-1425, the Company's program name, to the FDA.

The Phase 2 clinical trial will be a multi-center, open-label trial exploring safety and efficacy in relapsed or refractory AML and relapsed high-risk MDS patients who have been prospectively selected using Syros' *RARA* biomarker. The trial is expected to enroll approximately 40 patients. The primary endpoint of the trial will be overall response rate. The trial will also assess pharmacodynamic markers, duration of response, safety and tolerability, survival and biomarker predictability.

Using its gene control platform, Syros identified subsets of AML and MDS patients whose tumors have a highly specialized regulatory region of non-coding DNA, known as a super-enhancer, associated with the *RARA* gene. Syros then identified a biomarker for the *RARA*-associated super-enhancer, which it found in approximately 25 percent of AML and MDS patient tissue samples. Preclinical studies show the *RARA* biomarker is predictive of response to treatment with TM-411 in AML cell lines and patient-derived xenograft (PDX) models of AML. Treatment with TM-411 was observed to inhibit cancer growth and prolong survival in PDX models of AML with the *RARA* biomarker but not in models of AML without

the biomarker. These data provide meaningful evidence that patients with the *RARA* biomarker may be promising candidates for treatment with TM-411 and support further development of TM-411 in these genomically defined patient populations.

※Tamibarotene
The retinoic acid derivative invented by Dr. Koichi Shudo at Faculty of Pharmacy at University of Tokyo exhibits stronger differentiation activity with improved stability and safety than the retinoid agents currently available. Tamibarotene was developed by Toko Pharmaceuticals and approved (Amnolake Tablet® 2 mg) for relapsed/refractory acute promyelocytic leukemia (APL) in Japan on April 11, 2005.

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