



July 18 , 2014

TMRC Co., Ltd.

TMRC reached a collaboration agreement with Children's Hospital Los Angeles (CHLA) to develop and commercialize TM-411 in neutropenia

On July 18, 2014, TMRC Co., Ltd. ("TMRC" Hisao Ekimoto President & CEO, Tokyo, Japan) entered into a collaboration agreement with Children's Hospital Los Angeles to develop TM-411 (tamibarotene) for a new indication, neutropenia.

Under the terms of the agreement, TMRC will conduct the collaborative development with CHLA and TMRC will have the exclusive right to commercialize TM-411 for use in combination with G-CSF for the prevention and treatment of neutropenia.

TMRC's development of TM-411 until now has been chiefly directed as an anti-cancer agent achieving tumor remission /elimination against various types of cancer. TMRC's new focus for TM-411 is its development as a supportive care agent to treat neutropenia caused by chemotherapy. TM-411 has a variety of cellular actions including anti-proliferative, apoptosis and differentiation inducing activities. TMRC's prior focus for TM-411 drug development centered on its anti-proliferation and apoptosis actions, while researchers at CHLA, noting its capacity to induce differentiation of certain granulocytic precursors, found the combination of TM-411 together with G-CSF enhanced regeneration of mature neutrophils following chemotherapy beyond what G-CSF achieved on its own in preclinical studies.

Since the half-life of a circulating neutrophil is less than a day, the process of replenishing sufficient numbers of mature neutrophils in peripheral circulation to combat infection must occur swiftly and efficiently from bone marrow to blood stream. G-CSF is found to increase the number of immature neutrophils (proliferation) originating from hematopoietic stem cells and granulocytic precursors, while TM-411 is found to efficiently induce mature neutrophil differentiation. Together, the novel combination of G-CSF and TM-411 acts to restore circulating mature neutrophils, and comprises a novel therapeutic strategy against chemotherapy-induced neutropenia.

※Tamibarotene

The retinoic acid derivative invented at Faculty of Pharmacy at University of Tokyo exhibit the strong 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.



※G-CSF (Granulocyte-Colony Stimulating Factor) product

The protein product made by recombinant gene technic enhance the neutrophil proliferation by stimulating the bone marrow. G-CSF product is used for the prevention and treatment for bone marrow suppression after cancer chemotherapy/radiation therapy and hematopoietic stem cell transplantation. Market size worldwide is more than US\$ 5 bill.

• TMRC Co., Ltd.

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Paid-in capital : Yen 50 Mil.
Representative : Hisao Ekimoto, Ph.D. (President &CEO)
Business activity : Development, Licensing and Marketing of innovative anti-cancer
Drugs
URL : <http://www.tmrc.co.jp/english/index.html>

• Children's Hospital Los Angeles

Head office : 4650 Sunset Blvd, Los Angeles, CA 90027, USA
President &CEO : Richard D. Cordova, FACHE
Children's Hospital Los Angeles has been named the best children's hospital on the West Coast and among the top five in the nation for clinical excellence with its selection to the prestigious U.S. News & World Report Honor Roll. Children's Hospital is home to The Saban Research Institute, one of the largest and most productive pediatric research facilities in the United States. Children's Hospital is also one of America's premier teaching hospitals through its affiliation since 1932 with the Keck School of Medicine of the University of Southern California.
URL : <http://www.chla.org/site/>

For contact on this press release

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