PRESSRELEASE

SHIONOGI

Shionogi Awarded the Imperial Invention Prize

OSAKA, Japan, June 4, 2024 - Shionogi & Co., Ltd. (Head Office: Osaka, Japan; Chief Executive Officer: Isao Teshirogi, Ph.D.; hereinafter, "Shionogi") announced that Shionogi was awarded the coveted "Imperial Invention Prize" and "Invention Implementation Achievement Award," in June 2024, for the invention of dolutegravir, the HIV integrase inhibitor.

This invention pertains to an anti-HIV (human immunodeficiency virus) drug that suppresses the proliferation of HIV, the virus responsible for acquired immunodeficiency syndrome (AIDS). The drug is a compound that inhibits the integrase enzyme originally encoded by HIV. Dolutegravir is an excellent anti-HIV drug, that solves many issues such as adverse reactions and the emergence of resistant viruses. Products containing dolutegravir* as the main ingredient are contributing to improving the quality of life for people living with HIV worldwide.

* Tivicay, Triumeq, Juluca, Dovato

SHIONOGI aims to continue to grow sustainably with society by addressing the needs of patients and the world, and by continuously creating innovations that solve a wide range of healthcare issues.
We are committed to transforming ourselves into a HaaS company that provides value beyond the traditional framework of treatment, and are working to deliver cutting-edge healthcare solutions created through innovation to as many people as possible, as expeditiously as possible.

About the National Commendation for Invention
The purpose of the National Commendation for Invention, which receives funding from the Imperial Family, is to encourage and foster inventions and contribute to the improvement of science and technology and the promotion of industry in Japan, by honoring those who have perfected outstanding inventions, those who have made efforts to implement them, and those who have contributed to the guidance, encouragement, and fostering of inventions. Among these, the "Imperial Invention Prize" is presented to the person who has completed the most outstanding invention, thus serving as the symbolic award of the National Invention Awards. In addition, the "Invention Implementation Achievement Award" is presented to the representative of the company or organization to which the inventor belongs if the recipient of the Imperial Invention Prize is a corporation.

Overview of the award
Award Recipient (Affiliation at the time of this award)
1: Imperial Invention Prize
Takashi Kawasuji (Shionogi & Co., Ltd.)
Yoshiyuki Taoda (Shionogi & Co., Ltd.)
Teruhiko Taishi (Shionogi & Co., Ltd.)
Brian Alvin Johns (Brii Biosciences)

2: Achievement Award
Isao Teshirogi (Chief Executive Officer, Shionogi & Co., Ltd.)

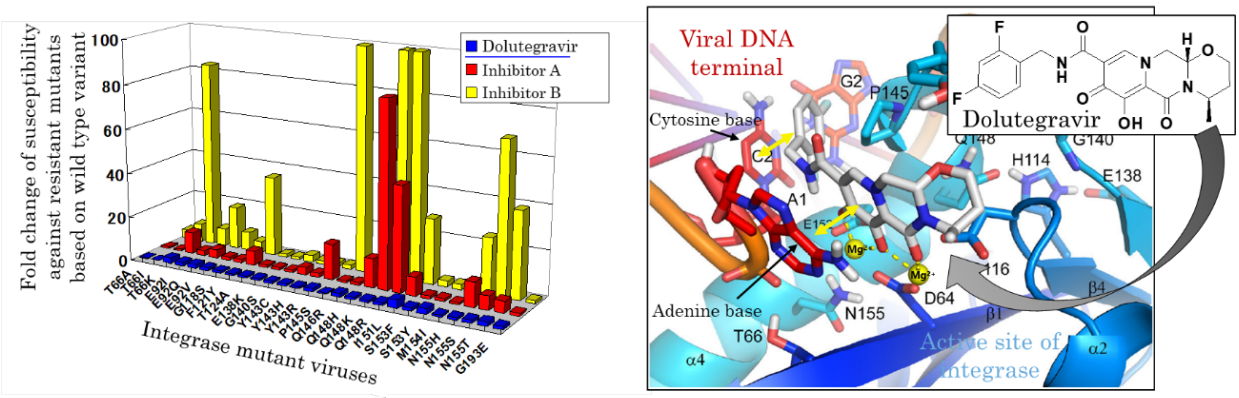
Award Name
Invention of Dolutegravir, the HIV Integrase Inhibitor

Overview of the Award-winning Invention

This invention relates to an anti-HIV (human immunodeficiency virus) drug that suppresses the proliferation of HIV, the virus responsible for acquired immunodeficiency syndrome (AIDS) The drug is a compound that inhibits the integrase enzyme originally encoded by HIV. Early anti-HIV drugs had complex dosage requirements due to the large number of tablets that had to be taken daily as well as drug interactions. They also presented many issues including adverse reactions and the emergence of resistant viruses, making it difficult to continue treatment.

At the time, inventors hypothesized that the inhibitory compounds were bound to two magnesium ions present in the active center of integrase. Combining this hypothesis with what they had learned from multiple failures, inventors continued to study the structure-activity relationship focusing on the binding affinity to the active center, and, finally, they discovered a unique compound with a tricyclic carbamoylpyridone structure that exhibited excellent antiviral activity. After structural optimization, they developed a compound that overcame the challenges, namely, dolutegravir.

Products containing dolutegravir as the main ingredient are approved globally and are recommended as the first choice of treatment. They also reduce resistant viruses and side effects, thereby improving treatment success rates and contributing to maintaining the health of people living with HIV.



Kobayashi. *et al. Antimicrob. Agents Chemother.* 2011 38:813–821. drawing from table 3

Deanda et al. *PLoS One.* 2013 Oct 16;8(10) drawing from Figure 2

Fig. 1, (left) Susceptibility of dolutegravir to integrase mutant viruses
(right) Structural model of dolutegravir binding to the complex of HIV integrase and a viral DNA terminal

Fig. 2 Four products related to dolutegravir

Forward-Looking Statements

This announcement contains forward-looking statements. These statements are based on expectations in light of the information currently available, assumptions that are subject to risks and uncertainties which could cause actual results to differ materially from these statements. Risks and uncertainties include general domestic and international economic conditions such as general industry and market conditions, and changes of interest rate and currency exchange rate. These risks and uncertainties particularly apply with respect to product-related forward-looking statements. Product risks and uncertainties include, but are not limited to, completion and discontinuation of clinical trials; obtaining regulatory approvals; claims and concerns about product safety and efficacy; technological advances; adverse outcome of important litigation; domestic and foreign healthcare reforms and changes of laws and regulations. Also for existing products, there are manufacturing and marketing risks, which include, but are not limited to, inability to build production capacity to meet demand, lack of availability of raw materials and entry of competitive products. The company disclaims any intention or obligation to update or revise any forward-looking statements whether as a result of new information, future events or otherwise.

For Further Information, Contact:

SHIONOGI Website Inquiry Form: https://www.shionogi.com/global/en/contact.html