Message from CEO

Bring Hope for Better Health through the infinitive Power of Science

We are a research- and development-driven company, focusing on the development of iPS cell-based regenerative medicine and the application of iPS cell technologies.

The Center for iPS Cell Research and Application (CiRA), Kyoto University and Takeda Pharmaceutical Company Limited launched the joint research program T-CiRA in 2015 to accelerate the research and advancement of iPS cell technologies as well as its application in regenerative medicine and drug development. For the purpose of transferring some of their outcomes into clinical practices as sustainable business, Orizuru Therapeutics Inc. was established in 2021.

Our portfolio is initially focused on two potential therapies researched in the T-CiRA program, one is with iPS cell-derived cardiomyocytes led by Project Leader Yoshinori Yoshida (Associate Professor at CiRA) and the other is with iPS cell-derived pancreatic islet cells led by Project Leader Taro Toyoda (Junior Associate Professor at CiRA). We will continue to seek other potential therapy where iPS cell technology may take a critical role. Another business scope is to support any drug discovery research activities and to build up iPS cell research platform based on our advancing iPS cell technologies.

We are comprised of over 50 staff who are either best-in-class researchers or in-depth expertise as technicians in the latest iPS cell technologies, even we are just being started. We have a mind in young, open and free, yet our heart is “to help society and patients per iPS cell technologies come from Japan.” That is the origin of our company’s name as Orizuru.

We inherit the scientific technologies of CiRA and Takeda, and will build new cultures on top of them here at Shonan iPark campus, Kanagawa, Japan. By providing regenerative medicines to patients, we will contribute to the future for medical practice, our people, and our society.

Kenji Nonaka

M.D., Ph.D.
President, Representative Director and CEO of Orizuru Therapeutics, Inc.

Qualifications

1990: Graduate Kyorin University, School of Medicine, and obtained Medical License
2002: Doctor Degree

Business career

1990~1994: Resident, Kyorin University Hospital, Departiment of Thoracic Surgery
1994~1996: Chief Resident, TORANOMON Hospital, Tokyo, Japan,
1996~1999: Staff, Kyorin University Hospital, Department of Cardiovascular Surgery, Tokyo Japan,
1999~2001: Instructor, Baylor College of Medicine, Department of Surgery, Houston, TX,
2002~2008: Research Director, Research Development Center, Banyu Pharmaceutical K.K. Tokyo Japan,
2008~2011: Director, Clinical R&D Department, Abbott Laboratories, Tokyo Japan,
2011~2016: Director, Head of Japan R&D, Abbvie Inc., Tokyo Japan,
2016~2021: Vice President, Head of Japan R&D, Janssen Pharmaceutical K.K., Tokyo Japan,

Company Overview

Orizuru Therapeutics promotes the social implementation of cell therapy products and innovative iPS cell iPS cell-related technologies (platform innovation).

Scope of Business	1. Development of regenerative medical products through cell transplantation. 2. Support for drug discovery research and development of regenerative medicine research infrastructure by utilizing iPS cell-related technologies.
Company Name	Orizuru Therapeutics, Inc.
Founded	April 9, 2021
Address	2-26-1 Muraoka-higashi, Fujisawa-shi, Kanagawa, 251-8555 Japan
Representative Director	Kenji Nonaka

Access

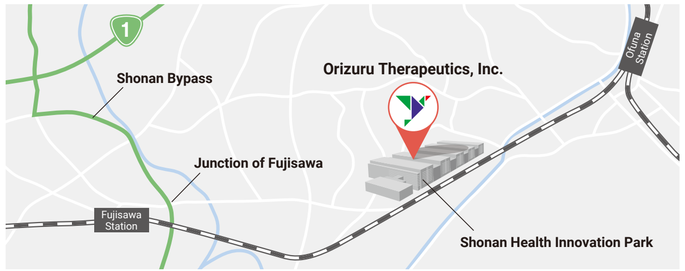
Location: Shonan Health Innovation Park, 2-26-1 Muraoka-higashi, Fujisawa-shi, Kanagawa, 251-8555 Japan

By train

From JR Ofuna Station: Take the Enoden Bus bound for Fujisawa Station Kitaguchi (bus stop No.1 at the East Exit bus terminal south of Lumine Wing)
and get off at Shonan iPark. (Approx. 15 mins)
From JR Fujisawa Station: Take the Enoden Bus bound for Ofuna Station Higashiguchi Shiki-no Mori (bus stop No.9 at the North Exit bus terminal)
and get off at Shonan iPark. (Approx. 15 mins)

By car

From Tokyo: About 11 km from the Kamiyabe Interchange on the Yokohama Bypass (Yokohama Shindo) via Route 1 Harajuku
From Odawara: About 6 km from the Fujisawa Interchange on the Shin-Shonan Bypass via Fujisawa-Bashi



https://orizuru-therapeutics.com/en/

ORIZURU THERAPEUTICS

Orizuru Therapeutics Inc.

Bring Hope for Better Health through the infinite Power of Science

iCM Project

We are developing a definitive therapy for severe heart failure patients with limited therapeutic options.

What is iCM

iCM is an iPS cell-derived cardiomyocyte created by a T-CiRA's project led by Dr. Yoshinori Yoshida, Associate Professor at Center for iPS Cell Research and Application (CiRA), Kyoto University. The myocardial differentiation method, which has been studied at CiRA, has been further improved towards practical use by using the cardiomyocytes purification method by small molecule compound discovered in the T-CiRA program. By transplanting iCMs, which are considered to be highly engraftable, pure and safe cardiomyocytes, into the patient's heart, they are expected to replenish the cardiomyocytes lost as the disease progresses and promotes remuscularization. Restoring the cardiac function of patients with severe heart failure, which has been considered difficult to treat, can be expected to improve the quality of life (QOL) and prognosis of these patients.

Our strength

Cardiomyocyte therapy requires the delivery of hundreds of millions of cardiomyocytes or more to patients. In order to provide cell products to patients with severe heart failure who are eagerly awaiting treatment, it is necessary to develop cell manufacturing technologies that can efficiently produce large numbers of cells. One of the most important technologies is a culture technique in which cells are suspended in a medium and cultured. We have been working since the early stage of development on a method for cardiomyocyte differentiation using a suspension culture system, which has been considered difficult to obtain high-quality cardiomyocytes. In addition, we have discovered unique small molecule compounds that efficiently remove non-cardiomyocytes generated during cardiac differentiation. By combining these state-of-art technologies with the differentiation method for preparing highly engraftable cardiomyocytes found in CiRA, high-performance, safe iCMs can be produced with a simple differentiation process. iCMs are highly effective when administered as single cells, eliminating the need for sheet or aggregate reformation. In addition, iCM is suitable for a wide range of administration methods, including catheter administration, enabling minimally invasive treatment with less burden on the patient.

Solution with iCM

Achievement of both high productivity and high purity.
Mass production-friendly suspension culture system. Removal of non-cardiomyocytes that could induce adverse effects, such as arrhythmia and cancer risk.

Stable supply to the people who need it when they need it.
Cryopreservable and off-the-shelf cell product

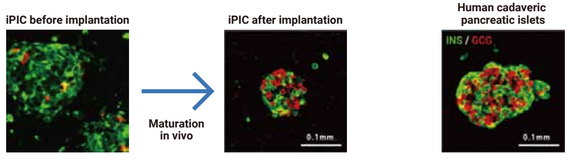
Assisting cardiac function for a long period of time.
High efficacy can be achieved by our highly efficient engraftable cardiomyocytes beyond the current drug therapy.

iPIC Project

We are developing a definitive therapy with iPS cell-derived pancreatic islet cells (iPICs) to brittle type 1 diabetes patients as a replacement therapy for islet transplantation.

What is iPIC

iPICs are human iPS cell-derived pancreatic islet cells expected to be suitable for cell therapy. They were discovered after a five-year optimization study through T-CiRA based on the pancreatic cell differentiation method (Stem Cell Res. 2015;14:185-97) discovered by Dr. Taro Toyoda, Junior Associate Professor at CiRA. iPIC is an aggregate of high-purity pancreatic endocrine cells that contains both insulin and NKX6.1 positive cells, which is a characteristic of pancreatic β cells. After implantation in vivo, pancreatic islet-like structures containing glucagon positive cells, another important endocrine cell type, are formed, and physiological insulin-secreting capabilities can be demonstrated in response to glucose loading and hypoglycemia.



Development of novel cell therapy product utilizing iPIC

To provide the novel treatment option to brittle type 1 diabetes patients, we have established the original subcutaneous implantation method that supports the long-term engraftment of iPIC. We then demonstrated proof-of-concept that implanted iPIC can treat diabetic rodents and pig models so far. High purity of expected endocrine cells, achieved by the combinatory approach of single-cell RNA sequencing-based transcriptomics and original compound-based purification, is one strength of our product. Fruitful collaboration with expertized equipment manufacturers enables us to yield billions of cells at one batch with a cell culture system optimized for iPIC. Now we are developing a product that can be supplied with the freeze-thaw tolerable iPIC for immediate use.

	iPS cells	iPS cell-derived islet-like cells (iPICs)	Subcutaneous implantation	Brittle Type 1 diabetes
Solution with iPIC				
	Unlimited supply	・**Scalable culture process** ・**Homogeneous and stable quality** ・**High purity**	・**Pancreas islet-like morphology** ・**Physiological insulin secretion** ・**Less invasive and retrievable surgery**	・**Freedom from hypoglycemic events** ・**Independence of insulin injection** ・**Minimization of immunosuppressant use**

Platform Innovation

We will promote innovation in drug discovery research and development of regenerative medicine by utilizing cutting-edge iPS cell technology.

What is Platform Innovation

By utilizing the cutting-edge iPS cell technology and the related technologies which have been cultivated through the T-CiRA program, we will support the creation of innovative pharmaceutical products through new drug discovery approaches and develop infrastructures for regenerative medicine research to provide iPS cell products at a reasonable cost and a stable supply.

Background of the Orizuru Therapeutics and T-CiRA

The discovery of induced pluripotent stem cells (iPS cells) in 2006 had a strong influence on the development of stem cell research and opened the infinite possibilities for drug discovery and regenerative medicine.
To develop clinical applications of iPS cells, Center for iPS Cell Research and Application (CiRA) at Kyoto University and Takeda Pharmaceutical Company Limited (Takeda) have been conducting "Takeda-CiRA Joint Program for iPS Cell Applications" (T-CiRA) since its agreement in 2015.
As the program progresses, a new framework is required to accelerate the realization of iPS cell-based therapeutics in a timely and effective manner, and Orizuru Therapeutics was established as one of the approaches. Orizuru Therapeutics, which inherited the iPS cell technology cultivated by T-CiRA and best-in-class researchers and technicians, will promote technological innovation and utilization of iPS cells and their related platforms, and contribute to the development of new therapeutic options.

T-CiRA Joint Research Program

Business development of candidate seeds through collaboration and commissioned business with other operating companies and university institutions

Solutions provided by iPS cell utilization technology

Consolidation of human resources who inherit the cutting-edge iPS cell utilization technology cultivated at T-CiRA

Production and analysis technologies for a wide variety of iPS cell-derived cells and tissue organoids

Support for drug discovery research utilizing iPS cell technology and development of regenerative medicine research platforms