



## Feature 1

# Realization of a Society of Healthy Longevity

### Back- ground

## Japan Faces with the Issue of Extending Healthy Longevity amid a Rapid Transition to a Super-Aged Society. We Are Steadily Expanding Areas Where Kampo Formulations Are Used

As Japanese society continues to age, the average lifespan has reached 84.07 years,\*<sup>1</sup> one of the longest in the world. However, there is a difference of around 10 years between the average lifespan and the average healthy lifespan,\*<sup>2</sup> and this remains an issue. Tsumura is focusing on this issue, and aims to contribute to the realization of a society of healthy longevity where individual people enjoy a well-balanced state of mind and body. One method of achieving this is to use the characteristics of Kampo medicines, with their ability to treat disorders at the pre-symptomatic stage of disease. We are striving to realize optimal Kampo treatment for each patient.

Recently in healthcare settings, the scope of diseases and treatment areas where the Company's prescription Kampo

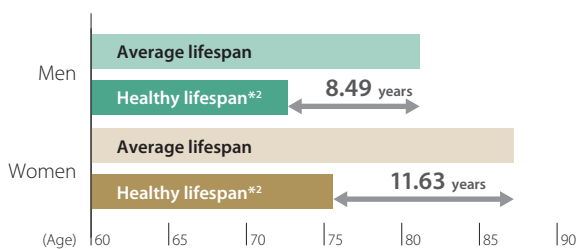
formulations are in use has been steadily expanding. For example, Goreisan, which regulates the balance of water\*<sup>3</sup> circulating in the body, is being more widely prescribed in the field of cardiovascular health to treat edema associated with heart failure. In addition, we are focusing on creating value in areas where we can make a significant contribution to healthy longevity, such as treatments to mitigate the side effects of chemotherapy drugs and for illnesses and symptoms that affect women.

\*1 The average value for men and women as of 2022 (Source: Cabinet Office, "Annual Report on the Aging Society 2024")

\*2 Average period of unrestricted daily living

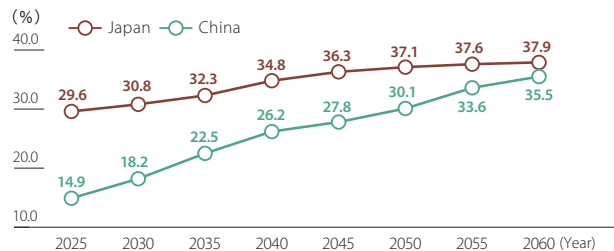
\*3 A concept in Kampo medicine that focuses on the metabolism of water in the body

### Disparity between Average Lifespan and Healthy Lifespan



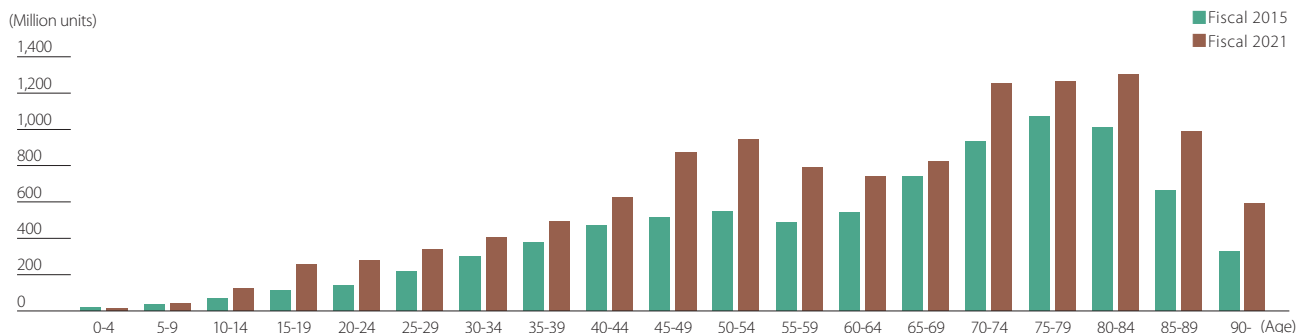
Source: Graph prepared by the Company from the Ministry of Health, Labour and Welfare, Health Service Bureau, Health Service Division's "Healthy Life Expectancy 2022 Data"

### Ratio of Population Aged 65 and Over (Estimated Values)



Source: Graph prepared by the Company based on Cabinet Office, "Annual Report on the Aging Society 2024," Chart 1-1-6

### Sharp Increase in Volume of Prescription Kampo Formulations Prescribed over the Past 6 Years, and 37% Increase in the Top Selling 100 Products



Source: Graph prepared by the Company from the Ministry of Health, Labour and Welfare's 2nd and 8th NDB Open Data

## We have identified three important domains and are collecting evidence with the aim of increasing new write-ups in treatment guidelines and recommendation levels

The Tsumura Group has set geriatric health, cancer (supportive care), and women's health as important domains, and we are continuously providing information related to basic and clinical evidence and use of different prescriptions, mainly regarding drug-fostering program formulations, "growing" formulations, and related formulations. By collecting evidence centered on the efficacy and safety of Kampo formulations, we are working to increase new write-ups in treatment guidelines and recommendation levels.

In the domain of geriatric health, we are conducting joint research with national research institutes and others on the themes of frailty, dementia, and cardiovascular disease.

In the cancer domain, we aim to alleviate the side effects from chemotherapy drugs and help patients to achieve improvements in physical condition and quality of life (QOL) through research relating to inflammation in the body, nutrition, and the immune system. In the domain of women's health, we are focusing on preconception care.\*4 We are working to contribute to women's active and lifelong health by focusing on the changes in women's life stages, such as menstrual symptoms and infertility.

Concentrating mainly on these important domains, we will produce papers and other articles of research evidence that provide the source for write-ups in treatment guidelines.

\*4 Addressing lifestyle and health from before pregnancy

### Expectations from People Outside the Company

#### The efficacy of Kampo formulations is palpable in clinical settings for geriatric medicine, the field of total care for seniors.

Dr. Sumito Ogawa

Professor, Geriatric Medicine,  
Graduate School of Medicine,  
The University of Tokyo



My field of specialization is geriatric medicine, a medical field that aims at health maintenance and QOL improvement for seniors. As the department of comprehensive medical care for seniors, the Department of Geriatric Medicine at The University of Tokyo Hospital specializes in total care that aims not only to make illnesses better, but to make patients better. Seniors tend to suffer from multiple diseases together, and to have a large number of medicines to take. Moreover, while the decline in their mental and physical functions can cause various distressing symptoms, such as urinary incontinence, dizziness, shortness of breath, decrease in appetite, and falling, many people do not know the cause. These are the patients whom we treat at the Department of Geriatric Medicine.

Kampo medicine focuses on the changes in physical and mental conditions associated with aging, and I have been keenly aware for some time that it has a strong connection with geriatric medicine. Recently, Kampo formulations of the type that have multiple components have been widely used for symptoms of deficiency syndrome\*5 and frailty. There are also cases where drug therapy centered on Kampo medicines has been used to address multiple symptoms. In other words, it seems that Kampo medicines are an effective way for seniors to avoid the use of multiple Western medicines.

I have personally felt the therapeutic effects of Kampo medicines in dealing with patients. The patients not only realize the improving effects on their symptoms for themselves, but in many cases the effects are also noticed by

family members who they live with or nursing care staff. I often hear feedback from family members saying that after starting treatment with Kampo medicines, the patient's appetite returned, or they began to talk more at home, or even that they have begun to smile more. Improving patients' drive and living functions like this also helps to relieve the burden on nursing care.

In our research activities, we have gathered a lot of evidence for therapeutic effects on symptoms seen with deficiency syndrome and frailty. Research using cells is also revealing the mechanism of action of Kampo medicines. I am hoping to see Tsumura deliver therapeutic effects on geriatric diseases through the concomitant use of Western and Kampo medicines, and through this, further effects from the combined use of non-drug treatments such as exercise and nutrition. Tsumura as a pharmaceutical company has the capabilities for promoting Kampo medicines and awareness of them overseas. As a means to achieve this, I think it is important for Tsumura to accelerate joint research with overseas companies, universities, and other partners. I also expect Tsumura to take action to deepen understanding across generations regarding the potential for using Kampo medicines for activities that support the enjoyment of living, social participation, and daily happiness of seniors. I believe Tsumura will play an increasing role going forward in helping to increase the value of Kampo formulations in geriatric medicine.

\*5 A concept expressing the physical makeup of a person, wherein their physical strength and resistance have declined, leaving them in a weak state

## Accelerate applied research towards establishing the most appropriate personalized Kampo treatment for individual patients, and realizing the scientific study of pre-symptomatic diseases

Tsumura's proprietary research package, KAMPOmics®, combines cutting-edge science, such as metabolome analysis,\*<sup>6</sup> transcriptome analysis,\*<sup>7</sup> intestinal flora analysis, and system biology,\*<sup>8</sup> to provide scientific clarification of Kampo. We aim to obtain an integrated understanding of the complex mechanism of action of multi-component Kampo medicines by promoting applied research on the most appropriate personalized Kampo treatment for individual patients and the scientific study of pre-symptomatic diseases. In the domain of personalization of Kampo treatment, we are working on development of a Kampo diagnostic support system that uses AI to support the analysis of common characteristics of patients for whom a certain Kampo medicine has a prominent effect and the diagnosis of patterns.

One example of this is a joint research project with Keio University on sensitivity to cold. As a result of analyzing factors such as the genetic background that contributes to cold hypersensitivity in adult women, in 2023, we discovered a genome area that is associated with cold hypersensitivity. Going forward, we will continue through this joint research

to identify genetic and physiological biomarkers relating to cold hypersensitivity, and objectively prove the association between Kampo prescriptions and their mechanisms of action. By doing so, we aim to establish standard diagnosis and treatment methods tailored to individual patients. Furthermore, we also envisage using this research to achieve social implementation of an evidence-based Kampo diagnostic support system.

Meanwhile, in our scientific study of pre-symptomatic diseases, we are accelerating initiatives to objectively evaluate the effects of pre-symptomatic treatment, prevention of aggravation, and prevention of relapses through research on biomarkers that define pre-symptomatic conditions. We will achieve social implementation of these research results in the form of proprietary technologies, and strengthen investments that lead to long-term value creation in the pre-symptomatic disease domain.

\*6 A field of research that performs comprehensive analysis of metabolites and Kampo medicine components within the body

\*7 Comprehensive analysis of gene expression

\*8 A field of research that seeks to provide a comprehensive explanation of biological functions by focusing on the interaction between genes, proteins, metabolites, and other biological factors

### Expectations from People Outside the Company

**We will clarify the concept of cold hypersensitivity, which does not exist in Western medicine, and promote understanding and treatment of this condition throughout the entire medical community.**

In Kampo medicine, a traditional diagnosis is performed based on the subjective complaint of the patient and physical signs. However, this approach is criticized as being unscientific, as it depends heavily on the experience and sensitivity of the individual physician. At the Center for Kampo Medicine, we are working with medical institutions nationwide to address this issue through a research project for objectively reviewing the Kampo diagnosis process and making it reproducible, even by a physician who is not a Kampo specialist.

In my own process of learning at a Kampo outpatient clinic, I discovered that many patients suffer from cold hypersensitivity. In particular, I was deeply impressed to see up close how the application of Kampo medicines was able to improve symptoms and give patients a real sense of QOL improvement. This experience gave me a strong desire to promote wider understanding of cold hypersensitivity and treatment methods throughout the entire medical community, and I started this research. In 2023, we conducted the first comprehensive genome analysis on the subjective symptoms of cold hypersensitivity, with approximately 1,200 consenting adult women as subjects. As a result, we

succeeded in identifying multiple genome areas associated with cold hypersensitivity. The results of this research were published in January 2024 in the international scientific journal *Scientific Reports*. Furthermore, we also applied for a patent based on the findings we obtained.

Through this research, we aim to show that the subjective complaint of cold hypersensitivity, which has long been handled by Kampo medicine, actually has a biological background, and to demonstrate the efficacy of Kampo medicines at the molecular level scientifically and medically. Ultimately, I would like to complete an objective medical interview system that all physicians can use, and build a medical foundation that is closely aligned to the symptoms of individual patients.

The appeal of Kampo medicine is its supportive approach in which the physician stays close to patients as a partner. Rather than simply eliminating disease, perspectives such as minimizing suffering and supporting better lifestyles will be essential for realizing a society of healthy longevity going forward. I believe that Kampo will play a supporting role in this.

#### Dr. Tetsuhiro Yoshino

Joint Research Laboratory  
for Precision Kampo Pattern Diagnosis,  
Center for Kampo Medicine,  
School of Medicine, Keio University



Tsumura is promoting joint research with Project Professor Norihiro Okada of the Laboratory of Genomics for Health and Longevity, School of Pharmacy, Kitasato University, to create evidence for realizing scientific study of pre-symptomatic diseases. In this research, we discovered the potential for intron retention<sup>\*9</sup> as a marker for pre-symptomatic diseases.

Furthermore, through clinical research, we have discovered that intron retention is an excellent marker for depression. Using these results, we aim to realize a society that assesses pre-symptomatic conditions and delivers early care and Kampo treatment.

<sup>\*9</sup> A phenomenon in which introns (the portions of the gene region that are not used for protein synthesis), which are normally spliced out, fail to be removed from the precursor mRNA (the transcription product of a gene) and remain in the mRNA

## Expectations from People Outside the Company

### Visualization of pre-symptomatic conditions by analysis of genes that cause intron retention and evaluation of Kampo medicines are now possible.

#### Dr. Norihiro Okada

Project Professor,  
Laboratory of Genomics  
for Health and Longevity,  
School of Pharmacy, Kitasato University



Not all of the various diseases that affect people have a clear associated biological pathway. For example, aging causes an attenuation of physical strength, dementia, and depression, which are currently difficult to treat with Western medicines. There are pre-symptomatic conditions for these diseases and symptoms, and there is room to create new value by improving pre-symptomatic diseases using Kampo medicines.

In autumn of 2024, a joint research project between Kitasato University's Laboratory of Genomics for Health and Longevity, School of Pharmacy, Oriental Medicine Research Center and Kitasato Institute Hospital discovered that intron retention (IR) is an excellent marker for depression.

Many researchers around the world have searched for markers of depression in the past, without success. However, in our research process, we have observed that when the body is stressed, IR occurs to maintain protein homeostasis, and that when the stress is alleviated by Kampo medicines, IR returns to a healthy status. Based on these accumulated observations, we

realized that genes in which IR is occurring could be used to evaluate depression status, or to evaluate drugs with an effect on depression, and we undertook further research. Now, our latest results demonstrate that IR is a versatile marker of diverse pre-symptomatic conditions. Furthermore, IR can also be used to evaluate the level of effect that Kampo medicines have on each type of pre-symptomatic disease by observing the recovery of IR. I believe that this result will have an extremely important meaning for the future of Kampo medicines, since they are effective in treating pre-symptomatic diseases.

Furthermore, in order to maintain stable efficacy of Kampo medicines, it is essential to continuously supply high-quality products with consistent composition. I believe that Tsumura's serious effort in this regard is extremely valuable. As the diverse information obtained from IR promotes the scientific study of pre-symptomatic diseases, I am certain that the value provided to society by Kampo medicines will increase going forward.

## Development of a Kampo Diagnostic Support System that Can Underpin Personalized Treatment

The Kampo diagnostic support system can carry out high-precision, science-backed diagnosis of patterns, which is considered to be in the realm of accomplished Kampo practitioners. Until now, we have worked on approaches such as registry research<sup>\*10</sup> using past treatment data, development of a prediction model for patterns, and accumulation of case studies. During the period of the second medium-term management plan, we conducted a verification test of the system in a clinical setting to increase its diagnostic accuracy.

With the development of this system, we aim to enable

the creation of objectified Kampo diagnostic methods (four diagnostic methods) and diagnosis by patterns. We also aim to contribute to increasing the overall quality and efficiency of Kampo prescriptions by physicians. It is also expected to be used as a training tool for physicians who are not Kampo specialists. We envisage the system being used to support physicians in clinical settings and as a Kampo education program for medical professionals. In the future, we will examine expanding the system beyond diagnostic support to include prescription proposal.

<sup>\*10</sup> Research that involves databasing and analyzing information on patients with certain diseases to obtain a deeper understanding of the diseases and improve treatment methods

## Working with a global viewpoint, we promote R&D to help address important healthcare issues.

Akihito Konda

CTO (Chief Technology Officer)  
Head of Research & Development Division



In April 2025, Tsumura merged its Research & Development Division and International Pharmaceutical Research & Development Division to enhance its development functions, including global operations, and installed me as the first CTO.

The newly integrated Research & Development Division created a vision of remaining close to our customers through all their life stages by meeting unmet medical needs\*<sup>11</sup> and building systems for addressing pre-symptomatic diseases along with a Kampo diagnostic support system, applying Kampo R&D with a global view. As an R&D organization, we ensure every researcher knows the areas of expertise of all other researchers so that they can go to the right person for help when needed. With that as a given, we strive to build work environments where all employees are self-motivated and encouraged to take appropriate action on their own initiative.

During our second medium-term management plan, we will conduct repeated clinical testing based on our research results in the fields of personalized health care (PHC) and pre-symptomatic disease and science (PDS), which are designated as priorities in our long-term management vision, and clarify the road map for social implementation of our offerings in these areas.

In global R&D, our first priority is progress with pharmaceutical development in the United States. We have long been watching postoperative ileus as an unmet medical need there. To treat it, we are developing and preparing to commercialize TU-100, an investigational new drug that shares the same ingredients with Tsumura's domestic product Daikenchuto. In May 2024, it entered the second phase of clinical testing with 402 cases in 36 US healthcare facilities. The United States is considered one of the world's hardest markets for advancing pharmaceuticals to commercial use, and we are embracing this challenge.

In the China business, our future growth driver, we are working to develop quality standards for the Kampo value chain, from cultivation of crude drug seedlings to final products, on a par with global standards set by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), and preparing to develop traditional Chinese medicinal products that meet these standards.

The Kampo diagnostic support system, which can be

a core support for growth of our domestic business, is now in the preparatory stage for clinical verification. The system is designed to standardize Kampo diagnosis, which requires Kampo medical knowledge and extensive experience. By supporting Kampo treatment based on clinical interviews with patients and pattern diagnosis, we project substantial contribution to the productivity of healthcare operations. We have also found a range of possible applications for the system, for example in creating training materials for healthcare professionals interested in Kampo medicine.

During the first medium-term management plan, we commenced joint research with Keio University and discovered a genetic factor that causes cold hypersensitivity. We then compiled the results into a method for diagnosing and classifying types of cold hypersensitivity and applied for a related patent in 2023. By leveraging our Kampo diagnostic support system with clear, scientifically grounded research results, we will gradually make progress in achieving our goals for PHC and PDS as designated in our long-term management vision.

*The Yellow Emperor's Classic of Internal Medicine*, known as the oldest Chinese book on medicine, explains that the wise practitioner addresses the pre-symptomatic disease rather than waiting to treat the resulting disease. In modern medicine, however, there is no established definition or indicator for "pre-symptomatic disease." So we think the effort to clearly define through evidence the concept of pre-symptomatic disease, which is a foundational component of Kampo medicine and Kampo drugs, will help develop the field of Kampo medicine and encourage the use of Kampo drugs. Above all else, we consider intron retention to be a promising research theme leading to the definition of pre-symptomatic disease. The results of research and analysis by Kitasato University have opened great possibilities for applying intron retention as a pre-symptomatic disease marker. In our second medium-term management plan, we will mainly conduct verification testing of Kampo methods and drugs related to depression and frailty with business and academic partners. At the same time, we will begin developing technologies for social implementation as testing services. We will continue R&D efforts to help address social issues, especially those related to women and seniors, through the scientific study of pre-symptomatic diseases.

\*11 Medical needs for which effective treatment has not yet been identified

# FOCUS Characteristics of the Kampo Market

## Domestic Market Trends

The majority of Kampo medicines prescribed at medical institutions in Japan are prescription Kampo formulations, which are covered by health insurance. A total of 148 prescriptions have been approved by the Japanese Ministry of Health, Labour and Welfare. Moreover, prescription Kampo formulations are prescribed based on examination by a physician, and they are now used in ordinary treatment by over 80%\*1 of physicians.

The market for prescription Kampo formulations has been expanding steadily since reaching its lowest point in fiscal 1999. In fiscal 2024, the scale of the prescription Kampo formulation market was 228.0 billion yen on a drug price basis, equivalent to approximately 2.0% of the 11.5 trillion yen prescription pharmaceutical market. The Tsumura Group holds an 84.6%\*2 share of the prescription Kampo market.

\*1 Source: Japan Kampo Medicines Manufacturers Association, "2011 Survey on the Status of Kampo Prescriptions"

\*2 Source: © 2025 by IQVIA. Compiled by the Company based on "JPM April 2024 to March 2025" (Unauthorized reproduction prohibited)

## Approach to the Market

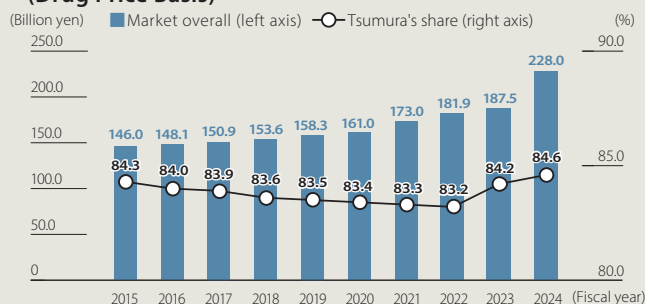
The Tsumura Group manufactures and sells 129 prescription Kampo formulations. With the leading lineup in Japan, we are able to respond to a wide range of treatment areas. Currently, our products are used in virtually every hospital department.

In addition, Kampo treatment is characterized by the use of various drugs to suit the constitution and condition of each individual patient. It is important to spread the knowledge of Kampo medicine so that even physicians who do not specialize in Kampo medicine are able to prescribe Kampo formulations. Therefore, in addition to providing information to medical professionals on the safety, efficacy, and quality of our products, our MRs also conduct activities to spread understanding about the establishment of formulations and

different uses based on the principles of Kampo medicine. In this way, we aim to realize a medical setting where all patients can receive Kampo treatment suited to them individually, regardless of the medical institution or clinical department.

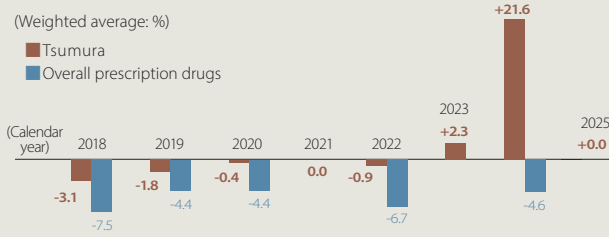
Moreover, over half of prescription Kampo formulations administered are for elderly patients aged 65 or over, and the ratio is higher for women of all ages, accounting for half the number of elderly patients aged 65 or over. The Group has designated as its key areas geriatric health, which is an acute social issue in Japan, cancer (supportive care), and women's health, and is striving to increase the quantity and quality of the information it provides.

## Prescription Kampo Formulation Market Trend (Drug Price Basis)



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## Changes in NHI Drug Price Revision Rates



Note: The revision rates for overall prescription drugs are not disclosed for 2021, 2023, and 2025 due to mid-year revisions.

## Domestic Business Product Lineup

