

Otsuka's Economic and Health Impact in the United States

2023–2024



Overview

ABOUT THIS REPORT

For the purposes of this report, Otsuka refers to Otsuka America Pharmaceutical, Inc., Otsuka Pharmaceutical Development & Commercialization, Inc., McQuade Center for Strategic Research & Development (MSRD), and Otsuka Precision Health, Inc. (OPHI), formerly known as Otsuka Digital Health (ODH), hereby referred to throughout the report as “Otsuka.”

This report focuses on the economic impact of the above organizations as well as the broader health and social impact of Otsuka in the US. This report, which is a collaboration between Matrix Global Advisors (MGA) and two Otsuka US subsidiary companies, measures the economic and health impact of Otsuka’s pharmaceutical business in the US. MGA is solely responsible for the results of the economic impact analysis presented in the report.

In addition to Otsuka’s contributions to improve clinical outcomes for patients and a strong commitment to the community, Otsuka’s US operations directly result in high-quality jobs, tax revenues, and economic output and indirectly support additional jobs and economic activity. MGA measures the full impact of Otsuka expenditures in the US economy using a macroeconomic model built by IMPLAN. The analysis was funded by Otsuka and conducted using Otsuka data. Otsuka had no role in the determination of results.

ABOUT OTSUKA

Otsuka is a healthcare company driven by its purpose and defined by its beliefs. At the core is perseverance, a fierce determination to overcome any obstacle regardless of setbacks, on behalf of patients and their loved ones. Otsuka is a leader in central nervous system (CNS) and nephrology, with both pharmaceuticals and digital healthcare solutions.

Founded in Japan in 1921, Otsuka Pharmaceutical Co. Ltd. today has an international network of 200 companies and approximately 47,000 employees across Asia-Pacific, America, Europe, and the Middle East. Operating in 32 countries and regions, Otsuka runs 175 manufacturing sites and has 44 affiliated research institutes. In 2022, Otsuka had revenues of \$13.2 billion and research and development spending of \$2.1 billion. More information about Otsuka can be found at www.otsuka-us.com.

ABOUT MGA

MGA is an economic consulting firm in Washington, DC. More information about MGA can be found at www.GetMGA.com.



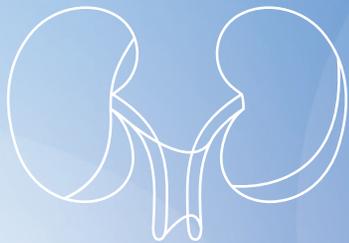
Otsuka in the United States

Otsuka Pharmaceutical Co. Ltd.'s first US commercial organization, Otsuka America Pharmaceutical, Inc. (OAPI), was established in 1989. With headquarters in Princeton, New Jersey, and corporate offices in Rockville, Maryland, OAPI oversees commercial activities in the United States.

In 2007, Otsuka Pharmaceutical Development & Commercialization, Inc. (OPDC) was established, with headquarters in Princeton, New Jersey. OPDC develops promising drug candidates from clinical trial management through planning the strategy for

drug approval, marketing, and lifecycle management.

Otsuka has nearly 2,000 employees in the United States working in all aspects of bringing new medicines to market, from research and development to commercialization. With a driving philosophy to serve those with unmet medical needs, Otsuka has a deep commitment to the development and commercialization of innovative products in the spaces of neuroscience, nephrology, and digital medicine.



Modeling Otsuka's Economic Impact

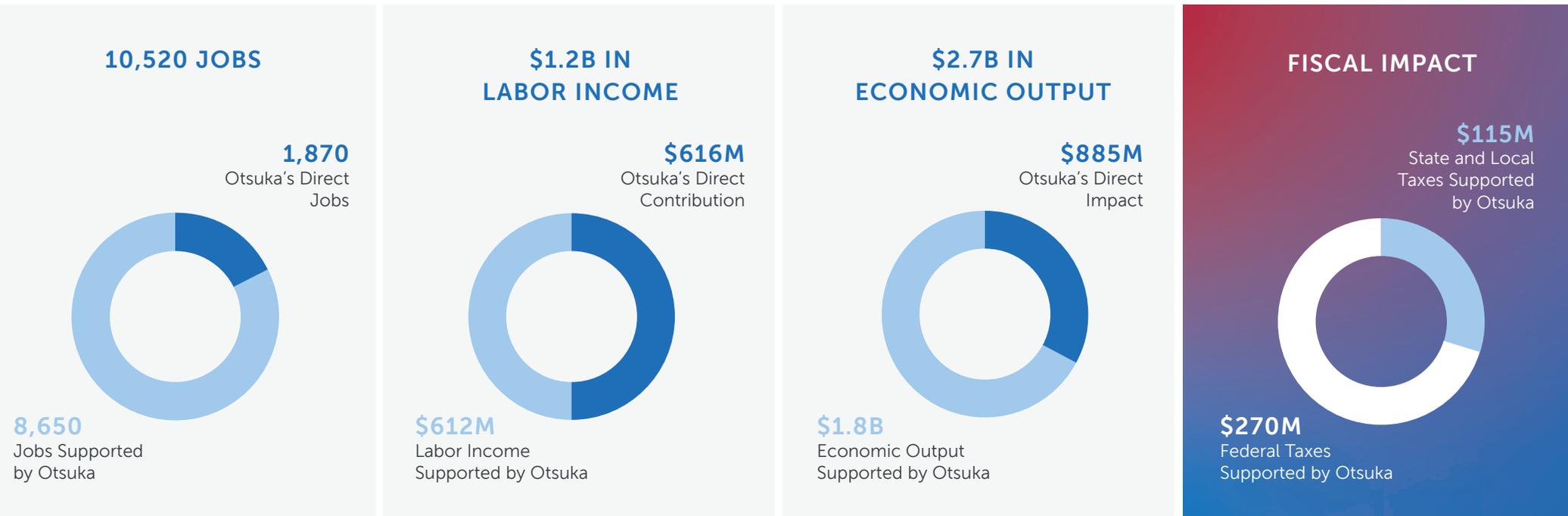
For the economic impact analysis presented in this report, MGA uses Otsuka's 2022 US payroll and operating expenses as inputs to an IMPLAN model of the US economy. IMPLAN's regional input-output models are widely used across government, academia, nonprofit, and corporate settings. Drawing on publicly available historical economic data for a specific region, the models project economic indicators (for example, production and employment levels) by industry.

Otsuka's Economic Impact

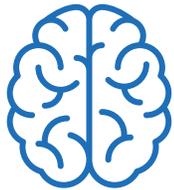
Beyond Otsuka's direct employment and spending in the United States, the company's operations support additional jobs, wages, and economic activity. Using a macroeconomic model of the United States constructed by IMPLAN, MGA estimates Otsuka's full economic impact by capturing the indirect income creation, spending, and re-spending that results from Otsuka's direct activity.

MGA's analysis finds that, in 2022, Otsuka supported 10,520 US jobs, generated \$1.2 billion in labor income (a measure of wages), and contributed \$2.7 billion in economic output. Otsuka also supports tax revenue in the United States. In 2022, tax receipts attributable to or supported by Otsuka's economic activity totaled \$385 million. (See Figure 1.)

FIGURE 1.
Otsuka's Economic and Fiscal Impact in the United States

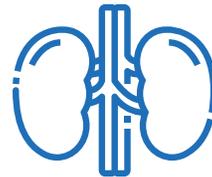


Otsuka's Therapeutic Areas of Focus



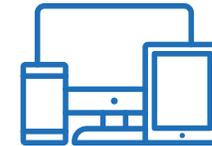
NEUROSCIENCE

In the US, 1 in 25 people has a serious mental illness.¹ The driving philosophy at Otsuka is to serve those with unmet medical needs, and that couldn't be truer than in Otsuka's dedication to the CNS space. In Otsuka's 30 years of experience working in this therapeutic area, the company continues to innovate and defy limitation by taking risks to overcome the complexities of treating mental health. Otsuka respects the value within every mind and is committed to making a difference in the lives of patients living with schizophrenia, major depressive disorder, bipolar disorder, and other CNS conditions.



NEPHROLOGY

For more than 20 years, Otsuka has been bringing its research and expertise to this therapeutic area. Otsuka has focused on developing novel drugs in areas of unmet need, such as autosomal dominant polycystic kidney disease (ADPKD) and hyponatremia, that have changed the treatment landscape. Otsuka's long-term perseverance has led to major breakthroughs, giving patients renewed hope and clinicians more treatment options. For example, Otsuka's treatment for ADPKD provided a first-in-class treatment option when it was approved in 2018 and remains the only available product. Otsuka continues to invest in the research and development of additional compounds assessing various forms of kidney disease.



DIGITAL INNOVATION

Digital technology has not only changed the world we live in, but it is also changing the face of healthcare. Otsuka is at the forefront of this transformative juncture in medicine, creating novel solutions that help address the challenges of those living with serious mental illness. Otsuka believes its investment and leadership in this therapeutic area will revolutionize patient care as we know it. Patients will be able to engage and communicate with their care teams in new ways, and clinicians will have data-driven insights that may help inform treatment decisions. By facilitating no-contact communication between patients and providers, digital medicine can provide a complementary offering to existing treatment and address unmet need.

¹ Centers for Disease Control (CDC), "About Mental Health," www.cdc.gov/mentalhealth/learn/index.htm.

Otsuka's Products

NEUROSCIENCE



OAPI co-promotes ABILIFY ASIMTUFII with H. Lundbeck, A/S



OAPI co-promotes REXULTI with H. Lundbeck, A/S



OAPI co-promotes ABILIFY MAINTENA with H. Lundbeck, A/S



DIGITAL MEDICINE AND THERAPEUTICS



NEPHROLOGY



Please see FULL PRESCRIBING INFORMATION including BOXED WARNING(S) for ABILIFY, ABILIFY ASIMTUFII, ABILIFY MAINTENA, ABILIFY MYCITE, JYNARQUE, NUEDEXTA, REXULTI, and SAMSCA at www.otsuka-us.com/products.

Case Study: Otsuka's Commitment to Diversity in Clinical Research

In working to bring treatments to those living with mental illness, Otsuka understands that it is critical to have diversity in research programs and clinical trials so that the outcomes are representative of the people Otsuka serves. Diversity in clinical research, particularly inclusion of underrepresented communities who may be most burdened, is important to ensure equitable access to interventional therapies that may offer more viable treatment options for patients.

² Karen Allison, Deepkumar Patel, and Ramandeep Kaur, "Assessing Multiple Factors Affecting Minority Participation in Clinical Trials: Development of the Clinical Trials Participation Barriers Survey," *Cureus* 14, no. 4 (April 2022): e24424.

³ Courtney P. Williams, Nicole Senft Everson, Nonniekaye Shelburne, and Wynne E. Norton, "Demographic and Health Behavior Factors Associated with Clinical Trial Invitation and Participation in the United States," *JAMA Network Open* 4, no. 9 (September 2021): e2127792.

⁴ The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard, "Diversity, Inclusion, and Equity in Clinical Research," www.mrctcenter.org/project/diversity-inclusion-and-equity-in-clinical-research.

⁵ Deloitte Center for Health Solutions and Pharmaceutical Research and Manufacturers of America, "Enhancing Clinical Trial Diversity: Stakeholder Perspectives on Advancing Research Through Representative Clinical Trials," *Deloitte Insights*, November 11, 2021.

FACTORS THAT ARE ASSOCIATED WITH A LOWER LIKELIHOOD OF PARTICIPATION IN TRIALS INCLUDE THOSE WHO:^{2,3}



Have language differences²



Have multiple comorbid conditions

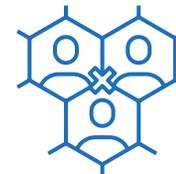


Reside in rural locations

LACK OF DIVERSITY IN CLINICAL TRIALS:^{4,5}



Hinders innovation and access to therapies



Limits both generalizable and subgroup-specific information about drug response and measures of safety and efficacy



Limits progress with improving public perceptions and building public confidence about drugs since others don't see and hear about clinical trial participants who look like them⁵

Otsuka's Approach

Research institutions holding clinical trials traditionally exist in cities or populated places, which can be a barrier for people living in rural areas. Committed to designing research programs that are fit for purpose and not one size fits all, Otsuka recently evaluated and changed clinical trial eligibility criteria and study procedures to be more inclusive of underrepresented populations.

In an effort to solve problems and decrease friction for patients while maintaining the focus on patient safety and data integrity that is central to its clinical studies, Otsuka has adopted program design elements including:

- Implementing telehealth capabilities when appropriate to ease the travel burden for patients and increase the catchment area of a study.
- Employing eConsent, which uses a multimedia approach to create a better-informed consent experience.
- Using remote data collection devices and apps to reduce human burden in data entry.
- Exploring the use of mobile units to conduct pre-screenings in communities and utilizing nontraditional sites, such as pharmacies.

Meanwhile, Otsuka's site engagement team works on:

- Promoting accessibility by exploring new geographical areas for trial sites, finding decentralized solutions to improve reach, and increasing the number of diverse investigators.
- Understanding the journey for healthcare providers to become investigators.
- Building relationships with new sites and maintaining relationships with existing sites.
- Understanding the challenges of different site types to develop best practices for site support.



THE PROMISE OF REMOTE CLINICAL TRIALS

Brick-and-mortar clinical sites will always be useful and necessary. However, the virtualization of clinical trials and the technologies that make them possible can help to broaden the number and types of medical centers engaged in clinical research. For example, Otsuka recently ran a fully remote trial for major depressive disorder, the Mirai Study, that was able to reach traditionally underserved and underrepresented communities.

The Mirai Study used Project Baseline, a remote clinical trial platform created by the precision health company Verily (formerly Google Life Sciences). Through this collaboration with Verily, Otsuka has been able to drive greater patient-centric research while remaining committed to ensuring patient safety, data integrity, and trial optimization.

LISTENING AND EDUCATING

As a company dedicated to serving those with unmet medical needs, Otsuka engages and collaborates early and often with affected communities to understand patient and stakeholder challenges—another important type of data. What Otsuka learns helps in crafting fit-for-purpose strategies and tactics to raise awareness about research opportunities and support recruitment and retention of study volunteers.

Otsuka released the DEIgest in 2021 to share how diversity and inclusion impact clinical trials. This digest was designed to bring awareness, insights, and optional resources to Otsuka's US active trial sites. The DEIgest is emailed to sites three times a year, covering topics such as LGBTQ+, disability, intersectionality, and socioeconomics, among others. The digest shares what Otsuka is doing internally and externally to help clinical trials be more diverse and inclusive, along with optional ideas and resources that site staff may use to incorporate diversity and inclusiveness in recruitment and at their sites. To date, Otsuka has reached more than 4,100 site staff at 898 different site locations in 46 US states.

In 2022, Otsuka launched a campaign to bring awareness about clinical research to populations that are typically underrepresented in such research. Otsuka representatives host booths at community events and conferences and share materials with community organizations. To date, Otsuka representatives have attended 24 community events and conferences and have reached more than 3,500 people.

In 2023, in collaboration with the Center for Information and Study on Clinical Research Participation (CISCRP), Otsuka created a "Diversity in Clinical Trials" video to explain what a clinical trial is and the importance of being inclusive and having diverse participants involved. A clip of this video has been shared on Otsuka's LinkedIn profile.

MAKING PROGRESS

Otsuka is supportive of recent policymaker focus on ensuring that there is diversity in clinical trials and including populations that have traditionally not been included in clinical trials, like the Medicaid population. Recent legislation requires that Medicaid programs cover the cost of clinical trial participation, which mirrors the requirement for other types of insurance coverage and will help ensure that the Medicaid population is included in clinical trials moving forward.

At clinical trial sites, steps to pursue diversity in clinical research and trials include:

- Engaging the community and local groups to promote awareness of clinical trials.
- Following Food and Drug Administration terminology for age, sex, gender, race, and ethnicity when collecting data.
- Building trust between participants and staff by employing a diverse workforce.
- Providing a safe space for participants from diverse backgrounds.

Otsuka's Pipeline

Otsuka is committed to the search for solutions for unmet medical needs. The company has therapeutics in all stages of development in CNS, nephrology, and other areas such as immune-mediated diseases and pulmonary tuberculosis. As of January 2024, Otsuka is conducting five Phase 1 trials, five Phase 2 trials, and six Phase 3 trials.

OTSUKA US INVESTIGATIONAL PIPELINE PROGRAMS

CNS		STATUS
Brexiprazole*	Post-traumatic stress disorder	Phase 3
AVP-786	Agitation in Alzheimer's disease	Phase 3
Centanafadine	Attention-deficit hyperactivity disorder	Phase 3
Centanafadine	Major depressive disorder (MDD)	Phase 2
OPC-214870	Epilepsy	Phase 2
OPC-224333	Epilepsy	Phase 1
SEP-363856 (ulotaront)»	Schizophrenia	Phase 3
SEP-363856 (ulotaront)»	Adjunct treatment for MDD	Phase 2
SEP-363856 (ulotaront)»	Generalized anxiety disorder	Phase 2
SEP-380135»	TBD	Phase 1
CT-152[^] (medical device)	Adjunct treatment for MDD	Filed

NEPHROLOGY		STATUS
Tolvaptan	Pediatric autosomal recessive polycystic kidney disease	Phase 3
Sibeprenlimab[§]	Immunoglobulin A nephropathy	Phase 3
VIS171[§]	Immune-mediated diseases	Phase 1
OPC-131461	TBD	Phase 1
VIS954[§]	TBD	Phase 1
OTHER AREAS		STATUS
Quabodepistat	Pulmonary tuberculosis	Phase 2

Note: In general, Otsuka discloses compounds that are in Phase 2 or a later stage of development, although some compounds in Phase 1 are disclosed in these tables.

* Part of Otsuka/Lundbeck alliance
» Part of Otsuka/Sumitomo Pharma America, Inc. (SMPA) alliance

§ Developed by Otsuka and Visterra, Inc.
^ In collaboration with Click Therapeutics
|| Supported by a grant from the Bill & Melinda Gates Foundation

Otsuka's Support for Patients

Otsuka offers a range of programs, featured below, that help patients in multiple ways, from financial assistance to mental health support to online resources.

COMMITMENT TO HEALTH EQUITY

Otsuka is committed to providing access to care and services for underserved patient communities to improve patient outcomes and support health equity. For example, Otsuka was the sole sponsor of the 2022 landmark report, "The Economic Burden of Mental Health Inequities in the United States," prepared by The Satcher Health Leadership Institute at Morehouse School of Medicine, a historically black college. Leading expert on the political determinants of health and health inequities, Daniel Dawes, was the principal investigator of the report. The purpose of the study is to close a gap in behavioral health and health equity research relative to mental health inequities. Otsuka also continues to support and drive policies across Medicare and

Medicaid focused on addressing systemic health inequity. We are encouraged by policymaker focus on creating policies, tools, data measurement, and other approaches to both identify and address health inequities.

ADDRESSING GAPS IN EARLY STAGES OF CARE

Otsuka is also focused on developing tools and services to bridge gaps in the early stages of care. For example, the company plans to work with advocacy partners to hold early screening events in communities. Otsuka also is looking at how digital interventions can help bridge gaps in early stages of care and drive early intervention.



Customer-centric support network of dedicated professionals and enhanced digital offerings striving to deliver efficient resolution to questions and challenges



Online educational resources across all of Otsuka's therapeutic areas for patients, families, and caregivers



A dedicated team committed to providing personalized access, affordability, and treatment-related support to patients, care partners, and their healthcare providers throughout their unique patient journey



Convenes traditional and non-traditional mental health stakeholders who are bringing innovative solutions to address critical needs in mental health



A community created for young adults to celebrate their minds, reclaim their lives from mental illness, share their stories, and seek support



Otsuka provides financial support to this separate 501(c)(3) nonprofit organization that provides eligible uninsured or underinsured patients with prescribed Otsuka medication free of cost

Otsuka's Work in Patient Advocacy

Otsuka actively collaborates with patient advocacy organizations to share ideas and insights and work to better understand patient and caregiver needs. Otsuka's work with these organizations is focused not on Otsuka products but on sharing perspectives, resources, and community relationships.

For example, Otsuka is an annual sponsor of the National Alliance on Mental Illness (NAMI) Family-to-Family program. Through its flagship program for educating loved ones of people with mental health conditions, NAMI provides eight free sessions

on a range of topics, including communicating effectively, finding local services, and handling crises. Otsuka is also a sponsor of Mental Health America's (MHA) annual Mental Health Month campaign, which spends the month of May raising awareness about mental health. Representatives from NAMI, MHA, and the Depression and Bipolar Support Alliance have been speakers and panelists at Otsuka-led summits and are steering committee members for NEXUS, one of Otsuka's mental health support programs.

Patient advocacy organizations Otsuka works with include:



Our Promise: We Are Committed to Walking Alongside Patients and Those Who Care for Them

At Otsuka, we believe patients are people first and we must deliver healthcare as human care. And to the families and care-partners on this journey, we are dedicated to standing with them, the way they stand with their loved ones—and offering the tools they need to care for the health of others and themselves.



Otsuka Pharmaceutical Affiliates

Otsuka has two pharmaceutical affiliates in the United States with different focuses pertaining to meeting patient needs:



MCQUADE CENTER FOR STRATEGIC RESEARCH & DEVELOPMENT (MSRD)

MSRD is a US limited-liability company started to identify and fund innovative early-stage research and development programs. These programs are the building blocks for future Otsuka products.



VISTERRA

Otsuka acquired Visterra in 2018 to continue developing solutions for unmet needs in nephrology. Visterra is a clinical-stage biotechnology company that is committed to developing innovative antibody-based therapies for patients with kidney diseases and other hard-to-treat conditions.

Otsuka Alliances

In addition to its affiliates, Otsuka works both internally and in collaboration with other companies to develop pharmaceuticals and digital innovations for nephrology and mental health.



CLICK THERAPEUTICS

With Otsuka's focus on digital innovation and unconventional thinking, its alliance with Click Therapeutics is a natural step toward developing solutions for patients that go beyond medication. We are working on developing and commercializing a prescription digital therapeutic for treating major depressive disorder. This alliance combines Click Therapeutics' specialization in discovering, validating, and deploying software applications with Otsuka's commitment and expertise in researching, developing, and commercializing treatments for mental illness. Together, we are breaking down barriers and have the potential to help transform mental healthcare.

LUNDBECK

Many pharmaceutical companies have experienced challenges when ushering in new CNS treatments. The Otsuka and Lundbeck global alliance agreement was born in 2011 out of this challenge. Both companies have a shared focus on helping patients with mental health disorders. Lundbeck has a long heritage of innovation in neuroscience, and Otsuka has been focusing research and development efforts on CNS for decades. Through this alliance, Otsuka and Lundbeck have taken an unconventional approach to develop and commercialize five psychiatric and neurologic therapies worldwide thus far. Together we are creating a positive impact to help improve the lives of people living with CNS disorders.

SUMITOMO PHARMA AMERICA, INC.

The global collaboration agreement between Sumitomo Pharma America, Inc. (SMPA) and Otsuka is focused on working on collaborative solutions to address these areas of unmet medical need, and will invest in advancing promising compounds while leveraging their complementary therapeutic area expertise. The goal of these co-development programs is to contribute to changing the course of serious medical conditions and provide new treatment options to patients and healthcare providers globally.

Otsuka's Social Impact

Otsuka provides financial support to its two nonprofit foundations and encourages employees to be active in their communities. The Otsuka Cares program represents Otsuka's commitment to making a difference. Through this program and interactive portal, Otsuka offers three unique ways for employees to get involved.

Otsuka people have always been passionate about helping others. We envision a world where everyone can access the healthcare they need. A place where every person living with a mental illness or other chronic disease feels supported and empowered to live life on their terms. It is our privilege to walk alongside our communities as allies and advocates to overcome barriers and reduce inequities. This is not just our promise, it is our passion.

We articulate this passion in three focus areas:



REDUCING STIGMA AND DISCRIMINATION

Otsuka supports nonprofit organizations and solutions that address and reduce stigma and discrimination toward those with mental illness, brain disease, or other chronic diseases.



INCREASING ACCESS TO CARE

Otsuka supports increasing access to treatment for those living with a mental illness, brain disease, or other chronic disease.



ADDRESSING SOCIAL DETERMINANTS OF HEALTH

Otsuka is committed to addressing economic and social factors that impact the health status and quality of life for people and communities.



Otsuka's Commitment to Scientific Advancement to Address Unmet Needs

The global Otsuka corporate family comprises science-driven companies with the corporate philosophy of:

“Otsuka-people creating new products for better health worldwide.”

Otsuka remains one of the only pharmaceutical companies that continues to tackle the unmet needs in mental illness. We do this across a variety of areas. We are continuing to invest in developing pharmaceuticals (pills and long-acting injectables), digital medicine, and digital therapeutics. We also believe that the need for innovative approaches to treating mental illness has never been greater. By recognizing the inherent value of every mind, we have the power to change the trajectory of people's lives. This is why we will not rest until mental illnesses and brain diseases are approached with the same priority and urgency as our physical health and recognized as chronic diseases that warrant early, equitable, and accessible intervention.

Otsuka is also a company willing to stay the course in bringing products to market. In CNS and nephrology, Otsuka has and continues to persevere in pursuing indications even if they require an extended period of time in clinical study. We know unmet needs across these disease areas are significant and the additional time is worth being able to bring new options to patients.



Otsuka's Dedication to Diversity, Equity, and Inclusion

At the heart of Otsuka's mission is a deep-rooted commitment to improving the lives of people of all races, ethnicities, genders, orientations, disabilities, and many other attributes.

Otsuka's employee groups include:



ABILITIES BEYOND LIMITS & EXPECTATIONS

Aids the company in recruiting and retaining individuals with disabilities by providing support that drives inclusion, equips, and empowers them and their allies to achieve excellence.



OTSUKA HOPE

Creates an open and inclusive environment where members and allies of the LGBTQIA+ community feel fully supported and accepted.



VETERANS ADVANCING LEADERSHIP, OPPORTUNITY & RESOURCES

A supportive community where veterans and their allies come together to foster camaraderie, share experiences, and provide valuable resources for personal and professional growth.



HISPANIC/LATINX OTSUKA LEADERSHIP & ADVANCEMENT (HOLA)

Supports the recruitment and retention of Hispanic/Latinx talent and provides opportunities for personal and professional development.



BLACK EMPLOYEE OTSUKA NETWORK FOR ENGAGEMENT (BEONE)

An Otsuka business and employee resource group that serves as an advisor to Otsuka's leadership to ensure meaningful representation by Otsuka's Black talent.



THE COMMUNITY WELL

Otsuka's peer-to-peer mental wellness group, a place to share stories and experiences, build community and connection, and reduce stigma and inspire hope.



INSPIRASIAN

Promotes cultural and heritage awareness of the Asian Pacific Islander community and supports the development and advancement of members and allies.



NETWORK OF OTSUKA WOMEN

Encourages and equips women to continue seeking positions of higher responsibility.

“If there is a single truth to overcoming the mental health challenges that America faces, it is that no one entity can do it alone. We must endeavor together to empower patients, further equity in care, and address barriers to access to offer renewed hope for those living with mental illness. A world where every mind is valued.”

– **Tarek Rabah**

President and Chief Executive Officer
Otsuka North America Pharmaceutical Business

We defy limitation, so that others can too.



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