Japan: triggering its next burst of innovation

Japanese innovation will be at the core of fourth industrial revolution technologies such as robotics and AI, as well as a new era of healthcare defined by regenerative medicine, next-generation pharmaceuticals and health supplements.

With the emergence of technologies such as AI, the Internet of Things and next-gen robotics, the world has entered a new era hailed as the fourth industrial revolution (or 'Industry 4.0'), while at the same time, major advancements being made in the fields of healthcare and renewable energy will potentially lead to a cleaner world and healthier and longer-living populations.

Simultaneously, Japan is undergoing a period of economic revitalization that is underpinned by technology and innovation. The consumer electronics and automobile industries played a major role in turning Japan into a global economic powerhouse in the 1970s and 80s, before the onset of the so-called "lost decades." But The Land of the Rising Sun is ready to rise again, leveraging on its technological pedigree to put itself at the forefront of Industry 4.0, renewable energy and healthcare.

Japan has the fastest aging population in the world. And while this population trend brings challenges, it is also seen as an incentive to boost innovation, not only in adopting Industry 4.0 technologies to address the nation's labor shortage, but also in the field of healthcare, where Japanese companies are leading advancements in areas such as regenerative medicine, next generation pharmaceuticals, elderly patient care, as well as in health supplements.

Japan is the first developed country to deal with the effects of a rapidly aging population and won't be the last. Hence what the world's third largest economy learns from this journey, it will be able to teach to others facing similar issues.

Aside from the development of new treatments and medicine for prevalent conditions such as cancer, diabetes, heart disease, among others, Japan's approach to healthcare also strategizes preventative solutions like health supplements.

"The Japanese are becoming extremely knowledgeable and meticulous about health supplements. This is in part because the government created preventative measures towards a healthier lifestyle, and that has been successfully injected into the medical sphere too," says Takahiko Nonogaki, president of heath supplement manufacturer, API.

"Of course, it opens an immense window of opportunities for us. Optimistically, we have been very successful in capturing the niche market and adapting our best practices in food manufacturing, while also implementing our new ideas for health supplements."

One of Japan's leading health supplement original equipment manufacturers (OEMs), API's fully integrated production system covers every process, from the procurement of high-quality ingredients to the manufacturing of the finished products. "With such a consistent manufacturing management system, we have the trust of major companies who choose API as a manufacturing contractor," adds Mr. Nonogaki.

Leveraging on its innovation and R&D capabilities in health supplements, API entered the pharmaceutical field in 2004 and today offers contract manufacturing and services in antibiotics, general active pharmaceutical ingredients and next-generation biopharmaceuticals.

Having opened its IKEDA Bio Pharmaceutical Plant in 2013, API aims to build contract drug manufacturing into a major business alongside its health supplements wing. Meanwhile, the adoption of Industry 4.0 technologies, such as AI, also form part of API's future strategy to develop better products as it looks to expand in the international market.

"We have the trust of major companies who choose API as a manufacturing contractor"

Takahiko Nonogaki, President, API Co., Ltd.

"We are confident that through our quality, formulations and ideas, we will be successful in the overseas market. We already have the know-how and solutions for health supplements, and are approaching new overseas customers," says Mr. Nonogaki.

"Furthermore, we would like to start having custom-made orders. This will require constant communication with the clients, but, like that, we are looking to further capture a new set of customers, and we believe we can be extremely successful.

"Lastly, we would like to start implementing AI, as accumulating data is a crucial factor in manufacturing supplements. It would allow us to have a clear understanding of the products that are being utilized by each client, and that will, therefore, allow us to understand the bestselling product line-up as well as the needs of our customers."

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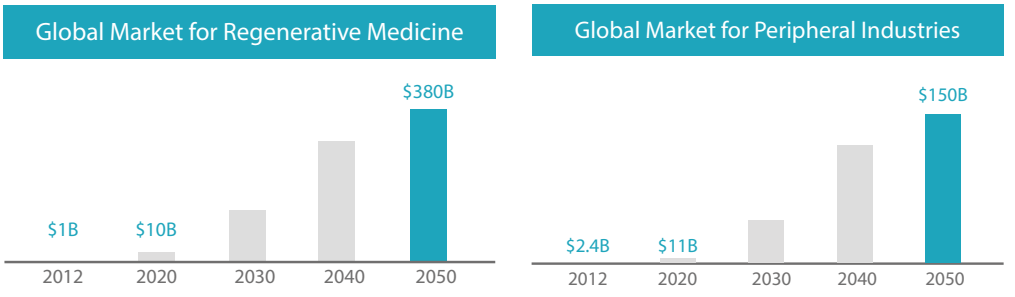
Pioneering the advancement of Regenerative Medicine

Japanese firm CellSource is an innovative new healthcare service provider pioneering the industrialization of regenerative medicine, one of the groundbreaking new fields in the global medical industry.



Source: Bio-Industry Division, Ministry of Economy, Trade and Industry, Japan (2015): "New Era of Regenerative Medicine With New Legal Framework"

Regenerative medicine – an interdisciplinary field combining engineering and life science principles to promote cell, tissue and organ regeneration – looks set to become one of the greatest developments in the medical industry in the 21st century and could revolutionize treatment over the coming years.

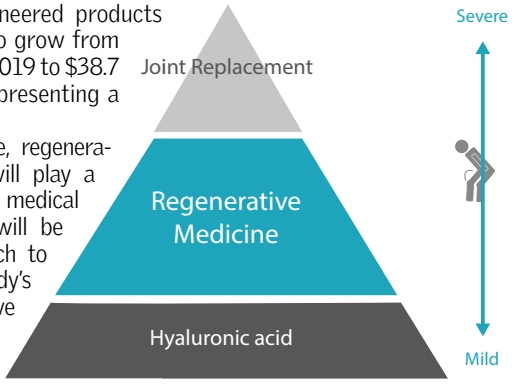
Amid the rapid rise in chronic diseases across the globe, as well as fast-aging populations in developed countries, regenerative medicine holds tremendous potential in the treatment of serious conditions including cancer, neurodegenerative disease, diabetes, heart disease, musculoskeletal disorders, and even respiratory failure caused by COVID-19 for which several FDA-approved clinical trials are ongoing.

With such rich potential to transform medical treatment, the regenerative medicine market – which is classified into cell-based immunotherapy & cell therapy products, gene therapy products, and tissue-engineered products – is projected to grow from $13.3 billion in 2019 to $38.7 billion 2024, representing a CAGR of 23.4%.

"In the future, regenerative medicine will play a vital role in the medical industry as it will be a novel approach to maximize the body's own regenerative capabilities and to prevent our organs from becoming permanently damaged. We hope to provide groundbreaking solutions for tissues and organs that may become severely damaged," says Masato Tsumamoto, CEO of CellSource, one of the pioneering Japanese firms in the regenerative medicine field.

Japan has been at the forefront of regenerative medicine innovation mainly due to two factors. First, the fact that Japan has the world's most aged population has prompted the country's healthcare industry to pursue novel approaches for the treatment of diseases generally associated with older age groups, such as those aforementioned. Second is the Sakigake System, the world's first regulatory framework implemented by the government in 2014 to promote the development of innovative medicine.

"In terms of R&D, clinical research/trials, and insurance coverage, Japan has created one of the most competitive ecosystems and has targeted innovative pharmaceuticals/medical devices which can treat and cure serious illnesses such as rare diseases and cancer," explains Mr. Tsumamoto. "Therefore, the Sakigake System has opened up a completely new field in medical services, enabling companies to industrialize regenerative medicine and to offer innovative treatments legally."



CellSource has developed regenerative medicine as a treatment for osteoarthritis.

> "By 2030, regenerative medicine will gain global popularity and CellSource will be at the center of this demand"
>
> Masato Tsumamoto, CEO, CellSource Co., Ltd.

It was amid this thriving new ecosystem for medical innovation that CellSource was established in 2015. Aside from the Sakigake System, the implementation of the Regenerative Medicine Act (RM Act) has enabled companies such as CellSource, which went public in 2019, to accelerate the industrialization of regenerative medicine in Japan.

CellSource's current business focuses on three areas: fat-derived stem cells, blood-based processing services and consulting services regarding regenerative medicine regulations, all of which fall under the company's comprehensive support platform that allows health professionals at its partner institutions to focus solely on patient care.

Under the RM Act, medical centers, who previously had to do all the handling and processing of cells themselves, can now outsource these procedures to CellSource, making the process more cost-efficient and providing these centers with more time to spend with patients.

"CellSource has collaborated with various medical institutions and research institutions to establish a state-of-the-art platform in regenerative medicine that is available for all to utilize," adds Mr. Tsumamoto.

"We are a new company which challenges to create universal value for the next generation while innovating without fear in today's rapidly changing society. We work on the industrialization of regenerative medicine and contribute to the development of society: 'In every life, regenerative medicine'."

Japan, of course, is not the only country facing grave healthcare issues due to an aging population. And moving forward, CellSource aims to expand its services overseas and satisfy the rapidly growing demand for regenerative medicine worldwide.

"Our mid-term strategy is to continue growing. Japan contains around 18,000 orthopedic clinics, and we only work with about 350 at this moment. This gives us a wide opportunity to continue growing exponentially in Japan," concludes Mr. Tsumamoto.

"We expect the value of regenerative medicine to be even higher by 2030, and it is for this exact reason that we expect CellSource to grow exponentially too. One of our goals for the next 10 years is to find overseas partners in order to export our services to the global market. By 2030, regenerative medicine will gain global popularity and CellSource will be at the center of this demand."

Aiming to be a Global Niche Top Company in Healthcare

Using the finest technologies, Alps Pharmaceutical extracts only the active ingredients from plants and herbs to develop high-quality pharmaceutical, food and cosmetic products.

"We are a company moving forward with a self-contained business, from the cultivation of medical plants through to the extraction of active components"

Osamu Ushimaru, President, Alps Pharmaceutical

The spectacular mountain range in Japan's Hida region, known as the Northern Alps, has long been valued for its rich abundance of native plants and herbs. And it is there where the roots of one of Japan's leading API (Active Pharmaceutical Ingredient) manufacturers can be traced.

Established in 1947 and borrowing its name from those same mountains where it began extracting herbs over seven decades ago, Alps Pharmaceutical combines its expertise in traditional medicine and prowess in modern science and innovation to turn nature's bounty into a vast range of pharmaceutical, food, supplements and cosmetic products.

Alps operates a fully integrated production model, farming high-quality medical plants right through to the final production of active ingredients using its own original purification technologies. Through its integrated skill, unique equipment and clever use of solvents, the company has been able to achieve extractions once seen as impossible. In particular, one of its strengths has been purifying solely the active ingredient from a natural plant extract, for example Sennoside from Senna and Capsaicin from chilli peppers.

"There is an episode supporting our integrated know-how. Kampo medicine is based on traditional Chinese medicine that was imported and developed in Japan in the 5th century and the most important characteristic is that it has many active components. However, the Japanese government strictly regulates the relative ratio of each active component and it is very difficult to comply with the specifications," explains president, Osamu Ushimaru.

Alps has long been supplying Big Pharma with a wide range of Kampo ingredients. But several years ago, one company attempted to produce some of these medicines by itself in China.

"We kindly gave information to encourage them to make these drugs but even then it was very difficult due to the surrounding regulations. They spent many years attempting to establish production, but it proved very difficult even with access to the same protocols," adds Mr. Ushimaru.

"Hence, it is our know-how that truly differentiates Alps from other companies. There is no special technology at Alps. Companies have similar technologies and that is why our technology itself is not unique, but nobody has our know-how in assembling technology. The power of assembling technology is at the core."

Alps holds the number one global market share for Capsaicin, which can be found in pain relief and psoriasis medication, and Sennosides, which are used in laxatives. Meanwhile, Rutin, a powerful anti-oxidant bioflavanoid contained in a wide variety of vegetables and fruits, and Glycyrrhizin, a flavoring agent in foodstuffs and cosmetics, are other products in which Alps holds a strong global market share.

But these are just four examples from Alps Pharmaceutical's enormous portfolio of products and extracts used by pharmaceutical, food and cosmetic manufacturers. Not only does Alps supply the highest-quality active components, it also works hand in hand with clients on the development and optimization of new pharmaceutical drug candidates, supporting them at every stage, from clinical trial to commercial production.

"Our company's mission is to supply high-quality drug substances at a low cost to encourage widespread use of our products. Even though our sales volume is somewhat small, when we factor in maintaining public health and addressing varying stages of health, our value add is at par with larger companies," says Mr. Ushimaru.

Alps is following a self-contained business model carried out by Merck (Germany) until the early 2000s, from the cultivation of medical plants through to the production of active components from those plants.

"This is an important strength for our goal to become a world-leading niche player," says Mr. Ushimaru. "However, we need another factor in addition to the self-contained business model, which is being a self-run business by developing our new own brand product. We are focusing on Alps' strengths – flavonoids, which are abundant in nature and have various biological functions."

Recently, natural flavonoids have attracted much attention across the pharmaceutical, cosmetic, and nutraceutical industries. However, these flavonoids have a significant problem in low water solubility, which typically exhibits as poor oral absorption and insufficient therapeutic effects.

"The market badly wants the high-solubility flavonoid. Therefore, the first thing was to develop a new practical method for producing compositions of flavonoids with improved water solubility. It took us three years during which solubility was enhanced by 2,000 times, which led to a significant improvement of oral absorption in a human clinical study," says Mr. Ushimaru.

"In this way we have developed a revolutionary product, named EubioFlavonoids™, as the first Alps brand product and also the first step towards our goal."

ACSL: Mile-high technology on auto-pilot

The fast-growing Japanese drone maker has developed its own autonomous flight control and SLAM technologies that allow its drones to be used in places beyond the reaches of GPS/GNSS-based competitors.

Japan's reputation for innovation, technology and high-quality has long been underpinned by corporate behemoths like Sony, Toyota, Mitsubishi Electric, tech giant Softbank and robotics manufacturer FANUC.

While innovation in the U.S is synonymous with the fertile landscape of Silicon Valley and the start-ups that have gone on to become major tech players, Japan does not have a global image as a teeming start-up hub. However, with many new companies involved in deep technology and engineering innovation, the nation's once-neglected start-up scene has begun to garner greater attention from venture capitalists and investors both at home and abroad.

Take, for example, drone manufacturer ACSL (Autonomous Control Systems Laboratory Ltd.), one of the few university-born start-ups that have managed to go public in Japan. Established in 2013 by a Chiba University professor with more than 20 years of experience in R&D of autonomous flying objects, ACSL manufactures autonomous drones based on the latest control system technologies.

Having secured multi-million-dollar investments from high profile sponsors, such as e-commerce giant Ratuken and The University of Tokyo Edge Capital, this exciting new company went public in December, 2018. "That made us the only publically listed specialized drone manufacturer in the world back then," recalls COO, Satoshi Washiya.

So what has investors so bullish about ACSL? Firstly, the projected growth of the global drone market, which is expected to surge to $43.1bn in 2024 (up from $14.4 in 2016) on the back of increasing demand from both business and hobbyist consumers. Growth of the market will also be supported by the rollout of 5G, which will significantly enhance the capabilities of drones and their utilization in industries across the board, from farming and construction to security and online shopping deliveries. Second is ACSL's competitive advantage over many other drone makers, namely its propriety control technologies and SLAM (Simultaneous Localization and Mapping) technology, which eliminates a dependence on GPS, thus, increasing the drone's autonomy.

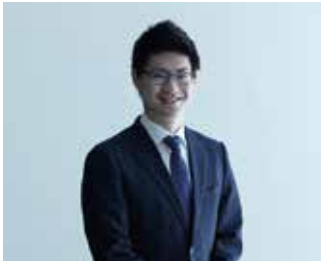
"There is a limited amount of companies that have their own control technology and can tailor to individual customer needs," says Mr. Washiya. "What we did at ACSL is build high-end-level autonomous drones without relying on external communication through SLAM technologies. We developed this proprietary visual SLAM system using cutting-edge machine-vision technology. With this system, ACSL's PF2-Vision drone, for example, can operate autonomously in a variety of settings that are not feasible using traditional GPS-based position sensing."

Hence, with SLAM built-in technology, ACSL's new PF2-Vision drone, which can fly at speeds of up to 70m/h and up to 50 minutes on auto-pilot, and the ACSL-Mini can navigate autonomously even in environments without any GPS/GNSS signals.

With the ACSL-Mini, SLAM provides precise measurements of the drone's position relative to recognizable features that it discovers in the environment, while its on-board 20MP, 30x optical zoom, gimbal-stabilized camera allows for the collection of high-quality images from hard-to-reach places.

"We've collaborated with Tohoku Electric Power and Nihon Unisys to do automated patrol inside a power generation facility. The reason we could do so is thanks to our SLAM technologies," says Mr. Washiya, adding that ACSL sees ample potential for its drones in three main areas: infrastructure inspection, deliveries and disaster reconnaissance.

Capital investment in ACSL has, in turn, empowered the company to invest in other developers of the latest autonomous flight control technologies. The Chiba-based company has already injected $3 million in U.S. firm, AutoModality, which has developed autonomous flight control software called 'Perceptive Navigation' that has gained global recognition.



"ACSL builds high-end-level autonomous drones without relying on external communication through SLAM technologies"

Satoshi Washiya, COO, ACSL

"The integration of AutoModality's 'Perceptive Navigation' technology into ACSL's integrated drone controls will enable autonomous flight in more complex and technically difficult GPS-denied environments. This integration will empower ACSL to capture further projects in such environments," explains Mr. Washiya, who also sees other potential investments in the pipeline, both in Japan and overseas, that would enable enhancement of the quality and reliability o f ACSL's drones.

Further M&A opportunities will form a vital part of ASCL's international growth strategy moving forward – as will a familiarization of the respective regulatory environments in target markets and finding other successful partnerships to boost its network.

"We are very open to strategic investment opportunities in any countries as long as it is beneficial," adds Mr. Washiya. "Ten years from now, I would like to tell you that ACSL drones have contributed to enhancing the quality of life for future generations."