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<u>This article was first published in The Business Times,</u> <u>Singapore on 13 February 2023</u> The pandemic has brought the spotlight onto the healthcare and biomedical sectors, driving unprecedented enthusiasm in the relatively unknown field of mRNA innovations, and bolstering growth in digital health. Yet, the silver lining has dulled investors' sentiments post-COVID. Increasingly, investors have become more cautious against macroeconomic headwinds, and many are expecting a correction in company valuations across all sectors.

ASIA REMAINS A BRIGHT SPOT AMIDST STORM OF UNCERTAINTY

2022 witnessed the harsh reality of bearish global markets with more pronounced impact for 2023. The global biotech industry had a tough year, with lower valuations, fewer successes in IPOs and waves of layoffs from biopharmaceutical firms.

Even as caution takes hold, there is still much undeployed capital or dry powder and active deal flow, particularly into Asia. Attracted by the sector's stable returns, resilience to recession and favourable demographic tailwinds, investors are still upbeat and positive about maturing healthcare assets in the pipeline.

In South-east Asia, increasing affluence of middle-income groups and governmental support make an attractive market for high quality and affordable healthcare. More patients in Asia are seeking better care as they value higher levels of comfort. While the sector remains fragmented, the appetite and willingness to spend in healthcare has drawn strong interest, including Chinese biomedical companies which are motivated to explore Southeast Asia as a potential growth market.

This year will be a challenging one with volatile financial markets, interest rate pressure, inflation, higher manufacturing costs and supply chain instability from geopolitical tensions. However, there are still pockets of investment opportunities in some sub-sectors.

As the biomedical sector undergoes a "reset" in the current financial downturn, this could present a golden opportunity for long-term equity driven investors to look at fundamentally sound companies with resilient balance sheets, backed by good science or impactful medical research at reasonable valuations.

Investors who prioritise value creation as part of their strategy in addition to financial returns will also play a vital role in shaping the region's biomedical sector in the coming years.

PATIENCE IS BITTER. BUT ITS FRUIT IS SWEET

Navigating the complex healthcare landscape and understanding scientific data can be extremely daunting. One common guiding principle is to identify areas with immense potential for technological advancement that fulfils unmet demand or provides a solution in the healthcare ecosystem.

In truth, investing in healthcare requires specialized knowledge for certain fields and a multifaceted approach that combines sound financial metrics, and a deep understanding on the underlying drivers that shape the entire healthcare ecosystem – from manufacturers to supply chain enablers, financial and insurance service providers to regulatory and policy makers. Adopting a forward-thinking mindset is also important in the strategy, along with a little luck, and loads of patience.

Patience and sustained commitment are crucial in healthcare and biomedical sciences investments. Typically, biomedical breakthroughs and research innovations have a long gestational period, showing successes over a decade or longer.

SINGAPORE'S EARLY INVESTMENTS IN THE BIOMEDICAL SECTOR PAVES THE WAY

Singapore's foray into biomedical sciences investments started almost 30 years ago with a holistic approach from building the necessary research and manufacturing infrastructure, attracting and nurturing biomedical talents, to catalysing private sector activities.

Bio*One Capital, a dedicated fund set up by the Singapore Economic Development Board (EDB) in the early 2000s, was instrumental in boosting domestic capabilities through its investments into over 50 local and overseas companies between 2001 and 2008. These early investments contributed to the transformation of the biomedical sector into one of Singapore's key economic pillars today.

Some notable investments that accelerated domestic capabilities in private sector research and development (R&D) and manufacturing included EDBI's partnership with Lonza, a Swiss multinational pharmaceutical manufacturing company to establish not one but two biologics manufacturing facility in Singapore, in 2006 and 2007 respectively; a joint venture with U.S. biotech firm Chiron Corp in 2000 that seeded S*Bio, Singapore's first biotech research company that spurred the development of small molecule drug discovery capabilities for new cancer assets, one of which was Pacritinib that gained FDA approval recently in 2022 to

treat blood cancer and bone marrow diseases; and in another investment in Fluidigm, a life science instrument company, which led to its first integrated fluidic circuit manufacturing hub in Singapore in 2005.

In another example, Singapore's first vaccine development startup Singvax was seeded back in 2005. Recognising its capabilities, Japanese pharmaceutical giant Takeda acquired the entity in 2013 and continued to grow the Singapore operations. The team developed various vaccine programmes including QDENGA - a dengue fever vaccine which is under trial in Singapore but gained approval for use in Indonesia and Europe in August and December 2022 respectively.

These pioneering projects kickstarted and built strategic capabilities which created a ripple effect that encouraged more biomedical startups to flourish and also attracted many large international pharmaceutical and biotechnology companies like Genentech and Illumina to build their facilities in Singapore, making the city state one of the leading biomedical research and manufacturing hubs for biologics and instrumentation in the world today.



Singapore's vision and efforts in the early years laid a solid foundation for the nation's ambition as the region's biomedical hub. According to data from the Ministry of Trade and Industry (MTI), Singapore's GDP grew by 5ingapore's GDP grew by 7.6% in 2021, making it one of the strongest economic recoveries in the world. The growth was driven by a combination of domestic and external factors, with biomedical cluster as one of the key contributors and having employed more than 25,000 workers.

DISTILLING LONG STAYING AND ACTIONABLE TRENDS

While current macroeconomic headwinds will help differentiate potential winners and losers, it is also important to identify areas ahead of the curve with a good potential for unrealised value. That means identifying companies that can build their solutions around long-term trends and enduring behaviours like how EDBI had identified mRNA technologies and digital health as having long-term potential impact. Companies like Moderna and Livongo are examples of such investments, and the commonality that underpins these investments is game-changing innovations and transformative solutions backed by solid research, technology and strong management teams.

Looking forward, the promising innovations that could blossom or intensify in the near to mid-term include:

Unlocking the superpowers of next-generation cell and gene therapies

Re-booting your immune system through genetic modifications of immune cells to treat degenerative diseases has become a reality. Since 2017, chimeric antigen receptor (CAR) T-cell therapies have achieved regulatory approvals in US, Europe and Asia, for its transformative potential to treat cancer.

Recognising the potential of this scientific advancement, Singapore's Agency for Science, Technology and Research (A*Star) and other institutes of higher learning have committed \$80 million to advance cell therapy research and development (R&D) and establish cell manufacturing facility with Good Manufacturing Practice (GMP) and Good Tissue Practice (GTP) accreditations to meet the rising demand for cell, tissue and gene therapy products.

As approved CAR-T cell products are limited to treating blood cancers, companies are developing next-generation cell therapies to navigate the complex tissue environment to eradicate solid cancers. Beyond the use of immune cells to treat cancers, cell therapies are also being tested for treatment of degenerative diseases such as Parkinson's Disease.



Once gene and cell therapies overcome manufacturing and scalability challenges, potentially using off-the-shelf therapies, this nascent field could fast evolve as a mainstream modality of medicine.

The AI and data revolution in digital therapeutics and precision medicines

Advancements in artificial intelligence (AI), big data and machine learning have made significant strides, but there is still untapped potential in its applications across the healthcare continuum.

Digitalisation of healthcare and lifestyle data has led to the emergence of digital therapeutics (DTx), a new class of therapeutic intervention to prevent, manage, or treat diseases using evidence-based software. As DTx gains momentum, medical care companies like Biofourmis come under the spotlight for its ability to use Al to continuously and remotely monitor patients, and personalised care individually, which could culminate in the future of healthcare management.

Another encouraging and emerging area is the advancement of AI and neural network architecture to mine aggregated molecular and medical datasets to accelerate drug discovery.

For example, Singapore-based Hummingbird Bioscience has leveraged computational biology through its Rational Antibody discovery platform to discover and advance precision medicines for cancer treatment. Engine Biosciences is another example – it uses its Al toolbox to decipher novel genetic networks in cancer and neurodegenerative diseases.

While AI and big data serving as enablers in the biomedical sectors seem to be on an upward trajectory, such advancements are still at their infancy and shrouded with challenges in integrating different data sources and types for meaningful insights. Other perennial issues like achieving data quality, getting health insurers endorsements, and maintaining crossborder medical data privacy protection rights also need to be addressed.

The advent of healthcare 3.0

Congruent to having more effective medicines, innovative healthcare models and technologies have also progressed as a crucial tool for preventive care, to keep the population healthy and away from the hospital.

One such use case is Singapore's key initiative Healthier SG that was launched in September 2022. It aims to transform healthcare delivery and support better patient care by making healthcare information more accessible, encouraging healthier lifestyles, and integrating healthcare data across the care continuum.

Early intervention could improve population health and this is where innovation and technology can play a crucial role such as in the diagnosis of diseases. For example, A*STAR, National University Hospital (NUH), Tan Tock Seng Hospital (TTSH) and biotech company MiRXES have discovered unique molecular signatures in blood that led to novel diagnostics for early detection of gastric cancer, allowing patients to seek medical treatment earlier.

Virtual care delivery is another area that shows immense potential. Spurred by the Covid-19 pandemic, adoption of digital healthcare tools is fast becoming a norm as shown by local tele-health service provider Doctor Anywhere which had expanded rapidly across the region.

As the world see a convergence in the areas of robotics, generative AI, predictive analytics, and advancement in medical diagnostic tools and remote healthcare wearables, the entire care continuum would benefit and the overall management of population health improve in the long run.

In the next decade, we envisage that individuals would be more empowered to take charge of their own health and be proactive in early intervention of chronic conditions. The global healthcare system will transform significantly to cater for better patient experience that is more accessible, affordable, holistic, and personalised.