FROM CONCEPT TO PRODUCT

THE KLARO™ COMMERCIALIZATION JOURNEY

HEALTHTECH INNOVATION
CASE STUDY SERIES

SINGAPORE BIODESIGN

sbenquiry@hq.a-star.edu.sg f sgbiodesign in sgbiodesign

HOST INSTITUTION:

Agency for Science, Technology and Research
SINGAPORE

GLOBAL AFFILIATE:

STANFORD BYERS CENTER FOR BIODESIGN

MAIN AUTHORS

Dr Kevin Koh

Founder & CEO
VIVO SURGICAL PTE LTD.

KEVIN is a medical technologist, entrepreneur, start-up mentor and angel investor with over 16 years of hands-on experience in various academic and commercial medical technology development settings.

Presently, he is Founder & CEO of Vivo Surgical (Singapore), an EN ISO 13485:2016 certified company specialising in the development and manufacture of next-generation surgical technology and robotic devices. The company's innovative products range from single-use in vivo surgical lighting to disposable endoscopic surgical robots, with FDA, CE and HSA accreditations recently attained for its KLARO™ flagship product.

Kevin was previously the Asia Investment Director for one of the UK's most established medical sciences private equity funds, where he was responsible for leading healthcare investments in Southeast Asia and the Middle East. Further to Kevin's experience in private equity and venture/growth capital fundraising, his other areas of commercial experience include corporate rebranding, marketing and operational restructuring.

Besides Vivo Surgical, Kevin's concurrent appointments include being Chairman of the Board of Directors of PathoVax, LLC (USA), Member of the Board of Directors of VerImmune, LLC (USA), Managing Director of Vivo Medical Holdings (Singapore) and Co-Founder & Executive Director of the Metropolitan Festival Orchestra (Singapore).

Kevin holds an MPhil & PhD in Biomedical Engineering from the Institute of Global Health Innovation at Imperial College London, a BSc (Honours) in Molecular Cell Biology from University College London, and a DipABRSM Diploma in Piano Performance from the Associated Board of the Royal Schools of Music (UK).

Mr Richard Lieu

Head of Technology
VIVO SURGICAL PTE LTD.

RICHARD is a medical technology innovator with 9 years of medical device development and commercialisation experience under his belt.

Currently Head of Technology at Vivo Surgical, an EN ISO 13485:2016 certified surgical technology and robotics company, Richard oversees each of the company's product lines with responsibilities spanning production, operations and R&D, to quality assurance and regulatory affairs.

Following past stints at Veolia and Siemens Medical Instruments, Richard was previously hand-picked to be the first clinical engineer of Singapore General Hospital's newly formed Device Development Office (DDO). Through his contribution and efforts, the DDO subsequently went on to become one of SingHealth's key research pillars – the SingHealth Medical Technology Office (MTO).

Whilst at DDO/MTO, Richard was tasked with bringing to fruition medical technology innovations originating from within the SingHealth ecosystem through application of the Stanford Biodesign process. Specifically, he was involved in several surgical technology projects as Co-Investigator, securing a total of S$2.5M+ in grant funding for proof of concept (POC) and proof of value (POV) development. As a further measure of success, several of these projects have been exclusively licensed out by medical device companies for full scale commercialisation.

Richard holds an MSc in Biomedical Engineering from Université Pierre et Marie Curie (Paris VI) and is a named inventor on 12 granted technology patents with several patents pending.

SINGAPORE BIODESIGN AUTHOR

Ms Fiona Loke

Senior Manager
Medical Technology Office (MTO) of SingHealth

FIONA is a Senior Manager with the Medical Technology Office (MTO) of SingHealth and concurrently consults as Curriculum Head for Singapore Biodesign. As Curriculum Head, Fiona works with the team to design materials for training innovators in the Biodesign approach and related topics via workshops, as well as in the Biodesign Fellowship. At MTO, Fiona and the team provide support to aspiring clinician innovators in unmet needs finding, solution generation, engineering management, quality management, regulatory guidance and commercialization planning, adapting the Biodesign methodology for medtech innovation in the local context.

Prior to this, Fiona worked in software engineering, leading a team developing healthcare applications combined with new media and providing training in healthcare interoperability standards. Fiona was part of the 2011 batch of Singapore Stanford Biodesign Fellows. She has also provided consultancy to A*STAR, Covidien (now Medtronic) and the Singapore General Hospital on medtech innovation.

Fiona is a named inventor on 5 granted patents, 3 pending patent applications and 3 PCT applications. 3 inventions are out-licensed and commercially available. She is also a WSQ ACLP-certified trainer. Fiona obtained B.S. and M.S. degrees in Electrical Engineering from Stanford University, with a focus in medical imaging.

FROMCONCEPT TO PRODUCT

THE KLARO™ COMMERCIALIZATION JOURNEY

Market commercialisation is every innovator's dream. After five years of development and commercialisation efforts, one group has done just that. In an interview with Singapore Biodesign ("**SB**"), the team from Vivo Surgical Private Limited ("**Team**") shares about the conceptualisation and developmental processes of KLARO™, an in vivo surgical lighting device.

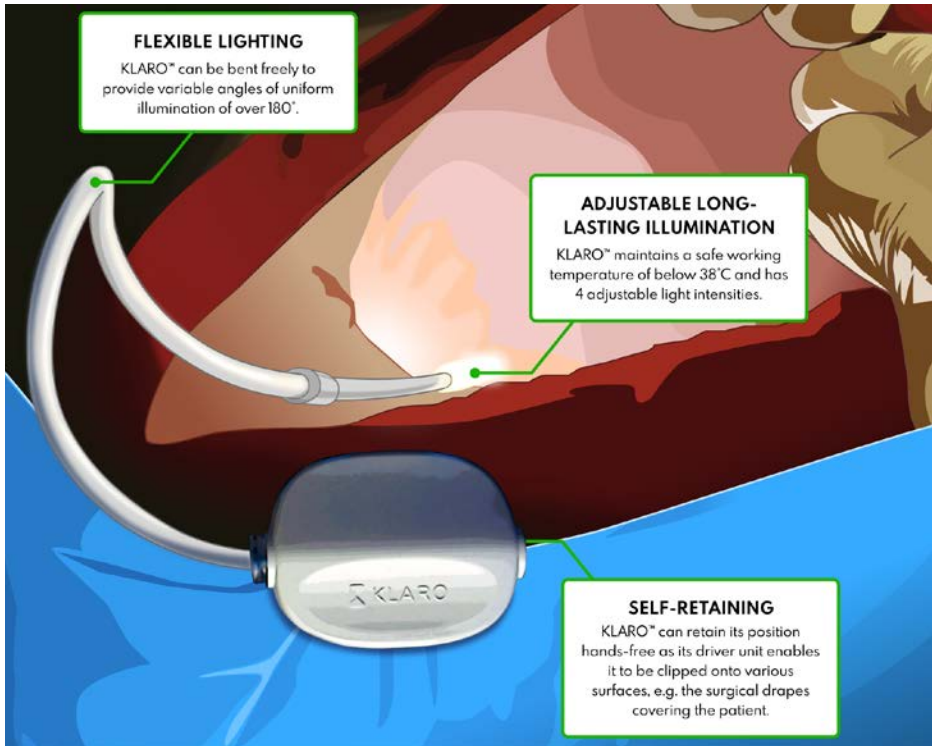

FIGURE 1: Diagram of KLARO™ Illumination Capabilities

QUESTION 1

SB: What are the intended use* and indications for use** of KLARO™?

TEAM: Surgeons have often articulated the need for better light sources to illuminate hard-to-reach regions, e.g., areas behind larger organs or sites that are oriented at difficult angles. In response, we have developed KLARO™, an in vivo surgical LED lighting device for use during open surgery. It is discreet, easy to use, and provides bright, uniform and localised "flood-lighting" from within open surgical sites. It is especially effective for illuminating deep open cavities and hard-to-reach regions where conventional light sources cannot sufficiently illuminate. In addition, since KLARO™ would already be providing sufficient illumination within the surgical cavity, surgeons would not need to perform such large open incisions to allow more external light into the wound. This in turn ensures faster patient recovery and markedly reduced scarring.

** Defined as the general use statement of a medical product or "what is the use of the device?*

***The conditions or reasons for using the device*

As **Figure 1** shows, KLARO™ comprises of a fully flexible 4.6mm diameter LED light strip and a clip-like driver unit. The LED light strip can be safely placed deep inside an open surgical cavity. It is freely bendable and provides variable angles of wide illumination of over 180°. The driver unit can be fastened onto surgical drapes during use. The entire device is a single-use disposable that maintains a working temperature of below 38°C over a 4-hour lifespan, ensuring sterility and zero tissue-burns. KLARO™ is, therefore, appropriate for most open surgery applications.

QUESTION 2

SB: What are the key development activities of KLARO™ from prototype to product?

TEAM: KLARO™'s development roadmap can be summarised in **Figure 2**.

Prototype to beta prototype (2 years)

Development work was undertaken primarily by SingHealth's Medical Technology Office ("**MTO**"). The key areas of focus were:

a. testing out device concept; and
b. assessment on fulfilment of users' needs.

The main objective of this stage was to determine device functions. For instance, levels of lighting intensity surgeons preferred, length of lighting tip and positioning of the device. At least three iterations of the prototypes were developed.

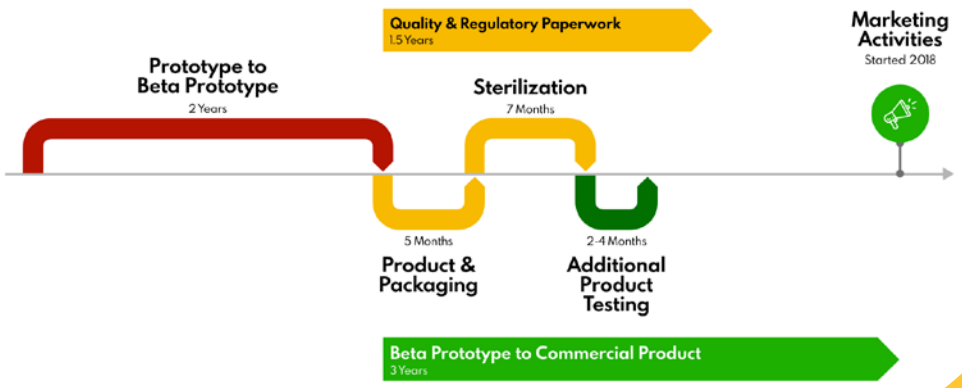

FIGURE 2: KLARO™ Development Roadmap

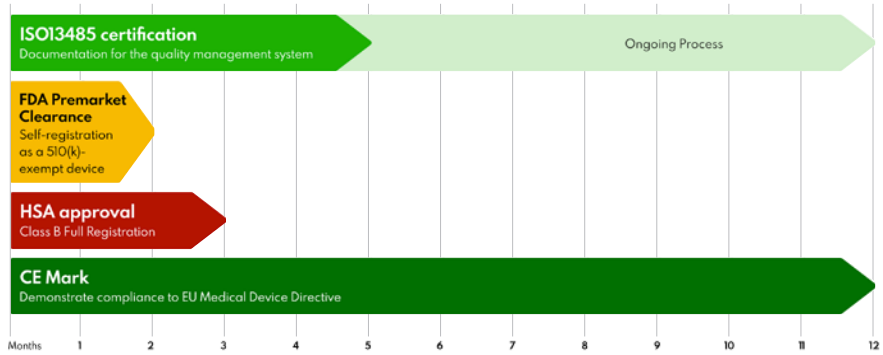

FIGURE 3: Timeline for Quality and Regulatory Activities

Beta prototype to commercial product (3 years)

Development work was spearheaded by Vivo Surgical Private Limited. The key activities included the following:

A. PRODUCT AND PACKAGING (5 MONTHS)

As the legal manufacturer for KLARO™, Vivo Surgical sourced for suppliers, produced samples and performed assembly with its manufacturing partner. User feedback was collected through a series of trials on animal models and cadavers, as well as interviews with end-users. The collated feedback was subsequently used to further refine the product specifications, leading to first article production, electrical safety testing and electromagnetic compatibility testing. For packaging, the team went through various phases, from design and assembly, to sealing and testing of the sterile packaging. This was conducted in parallel with product development.

B. STERILISATION (7 MONTHS)

Vivo Surgical worked with a third-party sterilisation house to perform validation studies. The results were used to obtain a sterile product, a sterile barrier (i.e., packaging) that could withstand the sterilisation process and a functioning product following sterilisation. Through these tests, we concluded that, of all the sterilisation methods, the electronics and battery-containing KLARO™ device could only be sterilised with ethylene oxide (i.e. EO or EtO) gas.

C. ADDITIONAL PRODUCT TESTING (2 TO 4 MONTHS PER TEST)

During this stage, the team conducted tests relating to biocompatibility, transportation, accelerated ageing and real-time ageing, amongst others.

D. QUALITY AND REGULATORY PAPERWORK (VARIOUS DURATIONS)

Given the nature of commercialisation work, documentation and planning (such as preparation of technical file) were performed concurrently with development activities. **Figure 3** will provide greater clarity on the regulatory requirements.

Marketing activities (started 2018)

Prior to commercial availability, KLARO™ had its soft launch at MEDICA[1] 2018 in Düsseldorf, Germany, to gauge early interest levels. Subsequently, KLARO™'s official commercial launch was at MEDICA 2019, where it garnered much interest from end-users and medical device distributors in several international territories.

Through the commercial development of KLARO™, the team has learnt the importance of executional timing, i.e., identifying activities that need to be undertaken at appropriate points in time. While some activities should be undertaken sequentially, others could be done in parallel. Good planning at this stage can expedite the process, with time saved ranging from months to years. For example, critical parts of the device should be ready when the device is sent for testing, as subsequent changes to these parts post-test may trigger yet another round of testing. In addition, if properly planned, most of the tests can even be conducted in parallel to achieve further time savings.

QUESTION 3

SB: How much was invested to bring KLARO™ from the licensing stage to the regulatory approval stage?

TEAM: Vivo Surgical invested more than SGD1,000,000 to bring the product from beta prototype to commercial product.

QUESTION 4

SB: How did Vivo Surgical bring KLARO™ through regulatory approvals with FDA, HSA and CE mark?

TEAM: Vivo Surgical hired two regulatory consultants to assist with the documentation for the CE mark audit. Once the audit was passed with no major non-conformities, Vivo Surgical proceeded to use the Technical File generated, as the baseline for FDA and HSA regulatory filings. For this particular medical device risk class, documents for both FDA and HSA regulatory filings were substantially similar to those that were submitted for the CE mark audit. The main difference being the presentation format for submission.

[1] *Singapore's enterprise development agency, Enterprise Singapore, leads a team of Singapore startups to MEDICA annually to showcase their innovations, gain distribution networks in Germany and Europe, and source for overseas partners. This opportunity enabled the team developing KLARO™ to understand its commercial potential with the European and international markets. This, and also served as a suitable platform to obtain commercial feedback for KLARO™.*

QUESTION 5

SB: What is the reimbursement strategy for KLARO™?

TEAM: Through conversations with key stakeholders (such as clinicians and distributors) across different international territories, it was clear that KLARO™ would not have its own reimbursement code. We envisage that it would be more feasible for hospitals to bill their patients for use of KLARO™. Depending on the territory, patients either foot their own bills or submit them to their insurance providers (for full reimbursement or co-payment). If KLARO™ were included in a procedure that is fully covered by the patient's insurance, then KLARO™ would, in a sense, be considered "reimbursable". (see **Figure 4**)

QUESTION 6

SB: How did your team decide which market(s) to access first?

TEAM: Our initial strategy was to enter territories where regulatory approval was not required. However, we learnt that end-users in these markets actually preferred to see KLARO™ approved for use in other territories first. As such, we modified our strategy to enter territories with the shortest regulatory approval timelines.

Another key determining factor was the unique requirements of the various territories. To decide which territory to access first, we obtained as much information as we could on the likely hurdles to commercialisation. These could include regulatory clearances, import procedures and licensing arrangements.

QUESTION 6

SB: For which activities did you source for Key Opinion Leaders ("KOLs")? How did Vivo Surgical convince the KOLs to support KLARO™?

TEAM: Vivo Surgical approached local KOLs and the company's network of clinician-collaborators to trial and/or champion KLARO™. Selected KOLs were also sought to contribute to the Clinical Evaluation file, which documents clinical evidence of KLARO™. Contributions from KOLs included analyses of KLARO™'s competitors, and pre-clinical trial protocols and results. The objective was to demonstrate KLARO™'s benefits to end-users and its competitive edge over current products on the market. In addition, Vivo Surgical also leveraged on the distributors' own networks of KOLs for support and publicity.

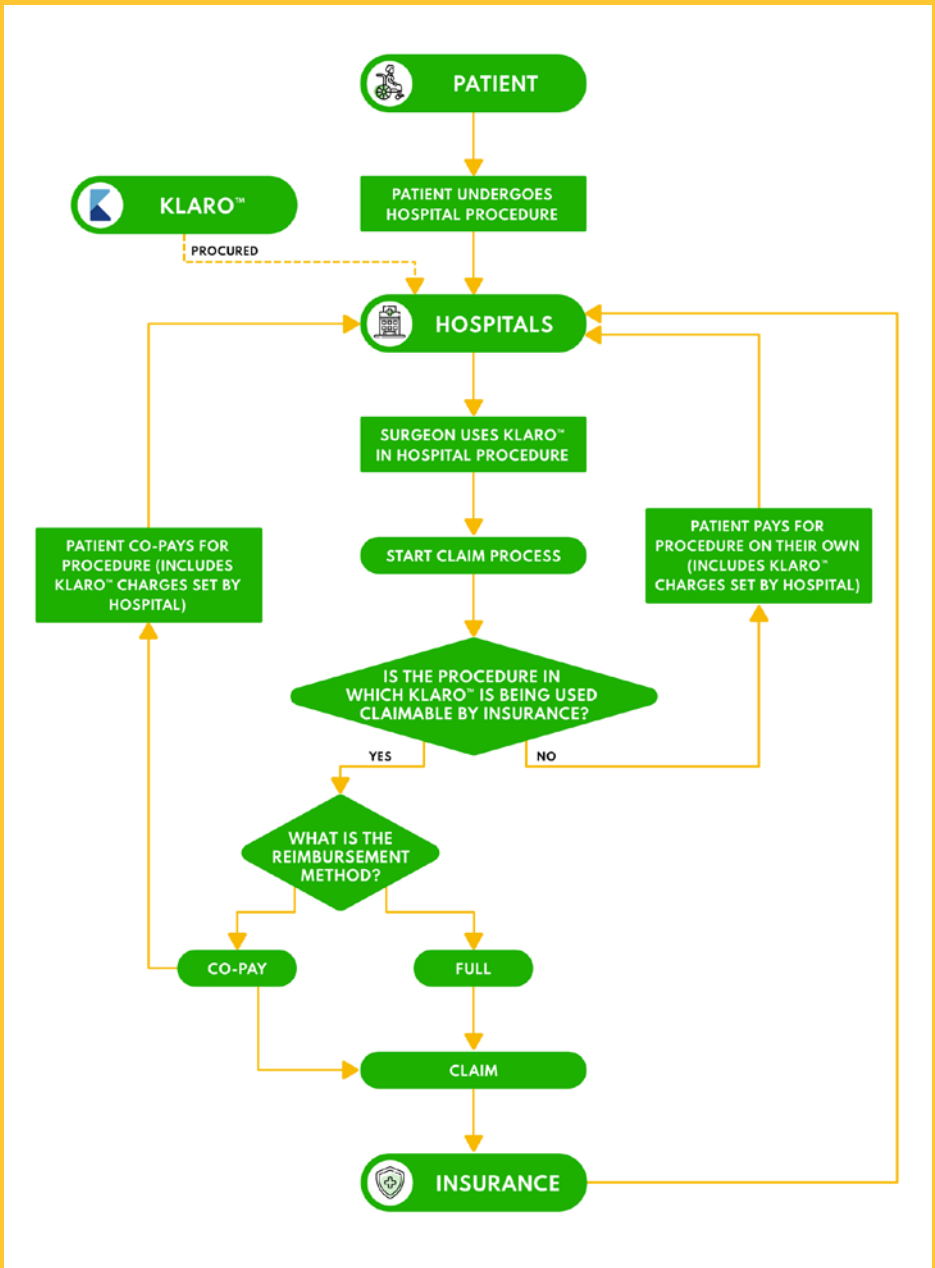

FIGURE 4: KLARO™ Reimbursement Strategy

QUESTION 7

SB: Between the research prototype and commercially ready product, what components and processes did you have to change?

TEAM: We had to make several, but necessary, changes to most of the research prototype's parts. This was largely due to KLARO™ being a single-use sterile medical device. As such, we had to minimise risks to the patient. All external facing parts of the device were manufactured with biocompatible medical grade materials, which would not have been present in the prototype.

Additionally, all parts used in the commercial-ready product had to be serial production ready, both quality-wise and material-wise. KLARO™ also had to undergo quality checks and in-process testing during production and assembly. The parts used in the prototypes, however, were typically from benchtop builds, CNC-machined or 3D printed, and would not have gone through such stringent tests and QC processes.

QUESTION 8

SB: What challenges did your team face in commercialising KLARO™? How did you overcome these challenges?

TEAM: One of the challenges faced was the lack of market presence, as we were entering the medical device marketplace with a new product. Following discussions with industry contacts and advisors, we decided to start with an exhibition booth at MEDICA (the world's largest medical device trade show), as well as attend the Arab Health trade show in Dubai (2nd largest in the world). The former focuses on the European/Asian markets, while the latter on the Middle Eastern/African markets. For both trade shows, we cast our network of distributors as wide as possible.

As for the US market, there are no large-scale medical device-focused trade shows, like MEDICA or Arab Health. There are, however, several smaller but more targeted workshops/conferences catering to a specific surgical specialty and/or select group of clinicians and end-users. Given that KLARO™ can be employed in multiple types of open surgeries, we need to assess and attend only the most appropriate and impactful conferences to optimise resources and time. We may also consider changing our approach for the US market, by approaching sales agents and distributors directly, instead of relying on trade shows for initial catchment.

Another challenge we encountered was effecting a mind-set change in clinicians, surgeons and end-users on how lighting is used in open surgeries. Currently, most surgeons use overhead lighting from headlamps or surgical booms. Given the conservative nature of the healthcare industry, clinicians generally prefer to maintain status quo, as even a minor change may be perceived as disruptive to the overall workflow. For example, it would probably require much convincing for senior surgeons to switch to KLARO™ for illumination. This is especially so, if they have already established a high level of confidence and familiarity in using conventional headlamps for performing surgeries.

To address this challenge, we provided end-users with relevant information in the form of comparison tables, product demonstration and KOL interview videos. We also provided KLARO™ samples to distributors for more effective demonstrations. We are planning for KOLs to evaluate sterile KLARO™ devices in live patients for a more definitive result. This would enable us to collect qualitative and quantitative feedback based on surgical discipline/type, light intensity and duration of surgery. We will also collate useful quotes from end-users to help us in communicating KLARO™'s benefits.

QUESTION 9

SB: Who are the key personnel a startup needs to take a product from the lab to commercialisation?

TEAM: Apart from the CEO, other key personnel would include, one whose key focus is technology, and another whose focus is quality assurance and regulatory affairs. The CEO drives business development, with support from the rest of the team. As startups are typically lean, all members would usually be involved in most of the developmental stages, to bring the product from lab to commercialisation.

QUESTION 10

SB: If you could refine any of the step(s) in KLARO™'s development or commercialisation, what would it be and why?

TEAM: While awaiting regulatory approvals, we proceeded to exhibit KLARO™ in 2018 and 2019, to gain a marketing and publicity headstart with potential distributors. Interested distributors were also issued non-sterile marketing samples to present to their KOLs. This approach, however, had its own challenges. Interested KOLs wanted to try sterile samples on patients in the Operating Theatre for more accurate results. Unfortunately, it was not possible to provide sterile units due to regulatory constraints. While we have obtained the relevant regulatory approvals by now, it has been more than a year of waiting for an actual sterile KLARO™ product. Some interested distributors (and their KOLs) who approached us back in 2018 would have already lost interest in the product. On hindsight, we could have identified a more opportune "sweet spot" along the commercialisation timeline to introduce KLARO™ to the market. That said, KLARO™ is a new product with many developmental unknowns, and it would certainly be challenging to identify the most ideal timing.

We had also spent substantial amount of time and resources in selecting the appropriate suppliers. KLARO™ is a medical device requiring stringent regulatory approvals and quality assurance. As such, once a supplier is confirmed, it is challenging for a start-up to switch suppliers. Such a change may be viewed as significant by regulatory agencies, requiring more (re)tests, substantial updating of the Technical File and possibly even another audit. On hindsight, we could have chosen to work with slightly more established suppliers or even have a back-up supplier for each component. However, this would come at a much higher cost that a start-up may not be able to afford.

CONCLUSION

1. It is important to identify key activities that will move your product towards commercialization and to be cognizant of the various timelines. Good planning is key to expedite the process.
2. To garner clinical adoption, your reimbursement strategy for your innovation needs to be robust. Although, the healthcare sector is fairly conservative in terms of innovation, there are various KOLs and agencies that innovators can leverage on to drive innovation forward.
3. Marketing, outreach, and resource allocation is important to ensure that your product or innovation is exposed to as many potential users as possible. However, there needs to be a strategy in rolling out these efforts to match with your productization timeline.

ACKNOWLEDGEMENTS

Dr Mary Kan
Programme Director

Mr Gobind Singh
Project Officer, Medtech Actuator

Dr Phin Peng Lee
Deputy Programme Director

Ms Karen Wong
Copywriter

Ms Preeti Mohan
Product Development Engineer

Mr Arfandi Azzahar
Graphic Designer

Mr Alex Choh
Innovation Training Manager

EMPOWERING ASIA'S HEALTHTECH INNOVATORS OF TOMORROW

Modelled after the established Biodesign Programme at Stanford University, Singapore Biodesign is a capability development initiative that aims to train and nurture the next generation of healthtech innovators for Asia.

We are a dedicated talent development and knowledge resource for health technology innovation, riding on the robust biodesign methodology and our wide-ranging regional network to provide an appreciation of healthcare needs through observations from stakeholder perspectives.

MISSION

High-touch development of healthtech talent centered on needs-based approach and quality industry mentoring to accelerate health technology innovation and adoption for Asia's* unmet healthcare needs.

VISION

To be Asia's* leading healthtech talent development and knowledge partner for accelerating health technologies innovation towards commercialization and adoption.

*Asia refers to SG, China and ASEAN

SINGAPORE BIODESIGN