DISCOVER
DEVELOP
COMMERCIALIZE
tomorrow’s health care
TODAY’S HEALTH CARE IS NOT GOOD ENOUGH.
Too many diseases have no treatment, much less a cure. Where therapies exist, they work for some, but not others. There is no way to know in advance which patients will win the treatment lottery. This hit-or-miss health care costs the system billions of dollars annually.

Every day, life-changing conversations are happening in doctors’ offices that underscore the urgent need for solutions. Patients aren’t asking for the impossible—just for some options
First-time parents absorb the just-delivered diagnosis: their toddler has leukemia.

With no time to lose, the boy immediately starts intense multi-stage chemotherapy, the standard of care, which involves 10 hospital stays over two years. It seems the cancer has receded, until, 12 months on, the oncologist tells the family their son's cancer has come back. Now five years old, the boy must undergo even more aggressive therapy or bone marrow transplantation. Neither comes with a guarantee; both will leave him with an immune system in ruins, vulnerable to life-threatening infections.
A 70-year-old woman, the heart of her family, is told, gently, she has Alzheimer’s disease.

She is flooded with terror that she will soon forget what it means to be herself, or who the people sitting in comfort with her now are. She doesn’t hear much else of what is said in that conversation with the well-meaning doctor, only that her disease has no cure.
A two-times Ironman qualifier learns multiple sclerosis is to blame for the scary symptoms he can no longer ignore.

His neurologist explains there are drugs that will reduce the number of relapses and help with symptoms, like intense nerve pain and muscle spasms, but that nothing will slow the progressive disease. Moreover, the 30-year-old will need to take the drugs and cope with their side effects for the rest of his life.
A new mom gets the results of the breast biopsy she has been awaiting: cancer, too big to remove.

Known for being positive come what may, today she feels only anxiety that her life, in some ways just begun, is out of her control. After juggling caring for her baby with six months of chemotherapy to shrink the tumour so surgery can be done, her doctor tells her she is one of the unlucky ones, that the chemo has had no effect. They will have to try radiotherapy. In the meanwhile, the tumour has grown, as has her distress and the gravity of her situation.
In each of these scenarios—and countless others—despite hearing different doctors at different hospitals deliver different diagnoses, each person also hears the same four words:

WE CAN FIX THAT.

In their quest to invent tomorrow’s health care, scientists at Sunnybrook Research Institute (SRI) are reshaping health care conversations, to get from today to the future. Scientists at SRI make discoveries. That’s only the starting point, however. Discoveries do not equal solutions; they have to get to hospitals, doctors and patients to have impact.

This is what sets SRI apart: It commercializes its discoveries, because that is the sole route to the medical marketplace—and thus to patients.

The innovations, the research—it is to find solutions for the people who urgently need them now. Scientists and clinicians work together, from the earliest phases, to make sure the pathway from the lab to the clinic is as clear and direct as possible.

Sunnybrook Research Institute has from the start had an entrepreneurial bent, as its track record in commercializing its discoveries shows.

Since 2000, it has launched 14 active startup companies. It doesn’t just want to make things a bit better. It wants to have impact at home and around the world, for all patients. Nothing less will do.

After years of discovery research and preclinical validation, SRI has dozens of therapies and technologies poised for the next leg of their journey to the medical marketplace. Six of these are on the commercialization cusp: Notch Therapeutics, Sonotype Dx, Vasomune Therapeutics, Precision Cancer Treatment, MOLLI Surgical and Next-Gen Focused Ultrasound.

These made-in-Canada innovations will make health care precise, predictive and personalized. They will save the medical system billions of dollars. They will deliver solutions for the most aggressive, even so-called untreatable, diseases. They will ensure each person in their greatest time of need hears: We can fix that.
Sunnybrook Research Institute commercializes its discoveries

10 PATENTS AND 6 LICENCE & OPTION AGREEMENTS PER YEAR issued to SRI in Europe and the U.S.

SUCCESSFUL SRI SPINOFFS
Calavera, Conavi Medical, Focused Ultrasound Instruments, FujiFilm VisualSonics, Harmonic Medical, Innovere, Profound Medical, Sentinelle Medical, Vasomune, Wave Check and XLV

$49M 2019 investment from the federal government into the Industry Consortium for Image-Guided Therapy (ICIGT), a pan-Canadian network led by SRI to develop and commercialize image-guided therapy technologies

$126M total project value of ICIGT, with added investment from private and public sector partners
The engineered T cell company providing the ultimate in precise, personalized medicine

NOTCH THERAPEUTICS

Therapies that harness the power of gene engineered T cells are saving lives, in some cases potentially curing once incurable diseases with a single dose. As these successes mount, the field for these therapies is growing rapidly, with clinical trials in play all over the world.

Despite the great promise of these therapies, there are major barriers to their wider use: Making them requires producing them from patients’ own cells, a slow and expensive process that produces uneven results.

Notch Therapeutics has invented a solution: a technology that can make gene edited T cells from stem cells on an industrial scale. It can make vast amounts of T cell therapies efficiently, consistently and to the same reliably high quality over and over again. It creates a scalable “off the shelf” option, thereby slashing costs and collapsing timelines.

Starting with a single gene edited stem cell, the technology enables cost effective large scale expansion into one trillion mature T cells that can be delivered as uniform cell therapy to thousands of patients, yet tailored to each one. Invented by an immunologist at SRI, the unique proprietary platform technology of Notch Therapeutics has extensive clinical applicability, positioning it strongly for leadership in the space.

The market includes the least treatable diseases: cancer, autoimmune diseases, infectious diseases, severe immune system depletion and organ transplant rejection. These are conditions without effective...
It starts with one gene-edited stem cell and ends in one trillion mature T cells that can be given as uniform cell therapy to treat disease in thousands of patients. The technology invented by Notch Therapeutics can make any of the designer T cell therapies, presenting a menu of scalable, “off-the-shelf” choices. Here, the streamlined expansion process to create pro-T cell therapy is depicted. Pro-T cell therapy has shown promise in conditions where there is high unmet need, for example, to regenerate immune systems destroyed by chemotherapy and radiation treatment for different forms of leukemia.

The technology’s market is boundless. It can be used to make all of the novel, designer T cell therapies hitting front pages around the world: chimeric antigen receptor T cell (CAR T) therapies, which are essentially curing patients with previously fatal forms of cancer; CAR Treg therapies, able to fight autoimmune diseases like multiple sclerosis, rheumatoid arthritis and Type 1 diabetes, and treat organ transplant rejection; transgenic T cell receptor therapies, for solid tumours in diseases like melanoma and gastrointestinal cancers; and Pro-T cell therapy, which can treat infectious diseases and rebuild the immune system from scratch.

A particularly huge unmet need is severe immune system devastation after chemotherapy and radiotherapy for leukemia. The technology invented by Notch is the first and only method that can reconstitute the immune system.

Notch Therapeutics’ incubation team has transferred the technology to a good manufacturing practices lab, where the cells can be made to the stringent purity required for human therapies. A world-first trial is being designed for people with advanced leukemia whose immune systems have been destroyed after receiving chemotherapy and radiation therapy. These results will lay the groundwork for clinical translation and commercialization within three years.
Almost 300,000 women receive a diagnosis of breast cancer in North America every year. Roughly one half will be assigned to standard of care chemotherapy, at a cost of about $50,000 each. Some might argue this is money well spent and it is if it works. The problem is, it doesn’t work in roughly 40% of these women. Apart from the unacceptable human impact, that’s a waste of $2.8 billion per year, a cost that will only climb as older adults continue to enter the system.

Time and money are thus squandered, while sick women get sicker, from the therapy and from the cancer that continues its insidious spread.

Sonotype Dx was invented by a scientist and radiation oncologist at Sunnybrook’s Odette Cancer Centre. The unique patented technology fuses artificial intelligence and ultrasound to let clinicians determine during a regular appointment if standard of care therapy will work before starting any treatment.

A woman visits her doctor upon finding a lump in her breast. She receives an ultrasound exam. Sonotype Dx immediately analyzes the data and generates treatment predictions. If the technology predicts the woman will respond to therapy, then it is full steam ahead. If it shows she will not respond, then she and her doctor can explore other options. This all happens during a single appointment, the woman’s first.

No other technology like it exists in the marketplace. Ultrasound is simple, portable and inexpensive. Within minutes, the test determines if a tumour is benign or malignant, and how aggressive it is; and predicts with
A woman finds a lump in her breast and visits her doctor. There, she receives an ultrasound exam. The data from the exam will show the doctor and patient if her tumour is cancerous and, if it is, how aggressive it is. Critically, the report generated by Sonotype Dx will also predict with 90% accuracy if she is likely to respond to standard chemotherapy or radiotherapy. One routine clinical appointment is all it takes.

Prospective clinical trials of the technology are underway in women with locally advanced breast cancer. Midway analyses affirm it is 90% accurate and sensitive. Final results are due in 2019. Initial testing is in breast cancer; however, the technology’s platform means it can be extended easily to other disease sites.

A team with clinical, engineering, manufacturing and commercial expertise is in place, with sales and marketing plans ready to execute. Based on the technology’s status as a proven prototype, the team is ramping up toward commercialization, with the first sale and deployment forecasted to happen within three years.

Sonotype Dx has no direct competitor. Functionally closest is a genomics test that examines surgically removed tissue to predict how likely it is that the cancer will return, and that can recommend if chemotherapy should proceed, but only in a nonspecific way. This gene-based test, however, costs thousands of dollars per patient; cannot predict if radiation therapy will work; cannot tell if a tumour is benign or malignant; takes 14 days to generate a report; and, critically, requires surgery. It thus doesn’t even approach the capabilities of Sonotype Dx.
Artificial intelligence-powered therapy: treating each patient as unique

In 2018, cancer killed 9.6 million people. This staggering statistic highlights a devastating truth: Effective treatment is elusive for far too many. About 50% of people do not respond to standard first-line therapies, like chemotherapy or radiation therapy. Targeted therapies, which attack gene mutations, are working better and helping people to live longer; however, for many patients, these therapies ultimately fail, too. Who these people are cannot be known until after therapy ends, with answers coming months, or longer, later.

The proprietary technology of Precision Cancer Treatment was invented in the lab of an SRI scientist who is a world leader in cancer biology. It marries a technique called high content imaging with artificial intelligence (AI) to identify in advance which therapy will work for which patient. It does so across a range of cancers, making it widely applicable.

First, a sample of live cells is taken from a person’s tumour. The sample undergoes high throughput drug screening where hundreds of drugs and drug combinations are tested at the same time for their tumour killing effect. An automated high content imaging system running 24/7 zeroes in on which drugs and combinations work, and produces a final report in just four days. With this report, doctors get patient customized therapy recommendations in which they can be confident, and patients don’t get potentially useless drugs and their horrible side effects. Instead, they get the best chance at life restorative treatment.
First, a blood sample is taken from a person's tumour. This sample undergoes high-throughput imaging, where an automated system running 24/7 screens hundreds of drugs alone and in combination for their tumour-killing ability. The system of Precision Cancer Treatment marries artificial intelligence with high-content imaging to produce a final report in just four days. The report recommends specific treatment for a specific patient—before any treatment has been given.

Along with peace of mind. Moreover, the health care system is spared the waste of paying for therapies that will not work.

Barriers to entry that protect Precision Cancer Treatment's market-ready position are its proprietary multichrome dyes and AI software, reprogramming technology and clinical trial data.

Based on robust preclinical and early clinical results, some of the largest pharmaceutical companies are using the technology to test the effectiveness of their drugs and to make better, more targeted drugs.

Clinical validation at Sunnybrook is ongoing, with trials in breast and lung cancer, chronic lymphocytic leukemia and acute myeloid leukemia. In North America, 600,000 people will be diagnosed with one of these kinds of cancer this year, and more than 240,000 people will die because of their disease.

As Precision Cancer Treatment moves toward commercialization, the team has partnered with a biotechnology company in China to refine and expand use of the technology. There, in just one year, the same four cancers arise in 3.8 million and kill 2.3 million people. With additional investment, the team will expand to service providers in China, ultimately rolling out the technology for worldwide impact.
Making tumour localization effective, efficient and globally available

Breast cancer cell with blebs (bulges of portions of the cell), captured by a coloured scanning electron micrograph.

MOLLI SURGICAL

During surgery to remove breast cancer tumours detectable only by imaging, ensuring the entire lesion is removed with enough of a margin to maximize the odds that all of the cancer cells have been removed, while maintaining a good cosmetic effect, is paramount. This can be difficult to do, which is why the need to repeat surgery to get cancer that was missed can approach 60%.

MOLLI is a handheld probe that helps surgeons find and remove a magnetic marker implanted into the tissue where a tumour is located. Conceived and developed at Sunnybrook, MOLLI stands for magnetic occult lesion localization instrument. It uses biocompatible rare earth magnets and sensitive detectors to let the surgeon know in 3D the precise position and depth of the tumour.

Doctors implant the marker at any time before surgery using ultrasound or mammography to guide the way. During surgery, the distance to the tumour is displayed on a monitor, and as the surgeon gets closer to it, an audible tone increases in pitch.

No other tool can do what MOLLI can do. Wire localization, today’s most commonly used technique, embeds a hooked wire into tissue. Results are variable, because the wire can move around or even be cut through, and patients find it painful. Furthermore, it has to be inserted on the same day as surgery, which is an inefficient use of hospital resources.
At any time before surgery to remove a breast tumour, a magnetic marker is implanted into the tissue using ultrasound or mammography. Later, during surgery, the doctor uses the MOLLI—magnetic occult lesion localization instrument—handheld probe to detect the marker. Visual and auditory cues tell the surgeon precisely where and how deep the tumour is located. This gives the surgeons confidence they are removing as many cancer cells as possible, while maintaining a good cosmetic effect.

Another common procedure inserts radioactive seeds to locate the tumour; however, the seeds can’t tell surgeons how deep to cut, and the signal can decay over time, making the seeds unreliable. Moreover, because they are radioactive, the seeds require special handling, which increases costs and prohibits some cancer programs from using them.

MOLLI has none of these handicaps. It alone can tell surgeons the precise depth of the tumour, bracket large tumours and identify multiple lesions that are closely spaced. The markers stay in place during surgery and don’t interfere with other instruments. MOLLI is easy for clinics to adopt because of its simplicity and cost-effectiveness. It requires no burdensome handling procedures.

It also offers a viable care option for clinics in lower-income countries, where surgery to remove breast lumps is not done because there is no reliable way to do it; instead, women in these countries typically have their entire breast removed.

Singularly versatile, the MOLLI system has market potential as a platform technology for use where accurate depth measurements during any kind of surgery are needed. Its first application, in breast cancer, is being evaluated in a first-in-human study at Sunnybrook. The trial is comparing MOLLI with radioactive seed localization, looking at safety, effectiveness and patient satisfaction. On the basis of results so far, the team anticipates the first commercial sale will happen in 2019.
Developing the next generation of medicines to maintain barrier defense and treat vascular dysfunction

It doesn’t get the public service announcements of cancer or heart disease, but vascular leakage is a serious, life threatening problem in many medical conditions. One of these is acute respiratory distress syndrome, or ARDS, which affects critically ill patients, typically in intensive care units (ICUs).

Here, the lungs become inflamed because fluid leaks from blood vessels into the lungs. This leakage prevents air from reaching the lungs, thus depriving the bloodstream of oxygen and sparking organ failure.

Of admissions to the ICU, 10% are due to ARDS. About 40% of people with ARDS in the ICU will die.

Decades long efforts to find a treatment have failed. Despite best efforts, there remain no drugs that can treat ARDS or the leaky vessels that are to blame. It’s an enormous unmet need.

Vasomune Therapeutics is an SRI spinoff founded in years of work and a breakthrough by an SRI cell biologist who discovered a compound that protects blood vessel health. This now late stage therapeutic stabilizes blood vessels so that they don’t leak. It also reverses the effects of inflammation caused by leaky vessels. Its foundational mechanism is involved in many disease states.
In many medical conditions, like acute respiratory distress syndrome and complications from diabetes, inflammation in the body goes into overdrive, causing blood vessels to become leaky, dangerously so. The late-stage therapeutic from Vasomune Therapeutics stops this from happening by binding to a cell receptor that puts the brake on runaway inflammation. Doing so restores the integrity and health of the previously leaky blood vessels. The drug, AV-001, also reverses the effects of the inflammatory attack.

Together, these conditions afflict millions of people at a high cost to individuals and societies. For ARDS alone, the global market is expected to exceed $2.5 billion U.S. annually.

A Tokyo-based biotechnology company that produces gene-based therapies has invested in Vasomune to co-develop the compound and get it into clinical trials. At first, it will be tested in ARDS, given the tremendous need there. Other indications being considered for co-development are asthma, glaucoma and vascular complications of diabetes, like diabetic retinopathy, which causes 10,000 people to go blind every year.

Vasomune and its industry partner will launch clinical trials to establish human proof of concept. Discussions are underway with the U.S. Food and Drug Administration on the design of the Phase 1 clinical trial, with an expected 2020 launch date. With this additional external scientific validation, the company will be positioned to take the compound to the next phase, commercializing it so it can get to the millions of people who have no other recourse.

The compound, AV-001, has been validated in preclinical studies, showing it works in ARDS, acute kidney injury, diabetic stroke and hemorrhagic shock, among others. On the strength of these results, it’s being developed for testing with people.
Diseases of the brain have the fewest treatment options and the worst outcomes. They cost families, health care systems and economies the most money. Many diseases, like amyotrophic lateral sclerosis (ALS), Alzheimer’s disease and inoperable brain cancer, have no treatment, much less a cure. Others, like essential tremor and depression, have treatments that control symptoms but often only for a short while.

Focused ultrasound (FUS) is a breakthrough technology. Pioneered by an SRI scientist and commercialized in partnership with industry, it uses sonic energy to exert a therapeutic effect on tissue. When used for scalp-free surgery, more than 1,000 sound waves are targeted to the region of interest under MRI guidance. The beams precisely destroy the unwanted tissue all without a single incision.

The commercial technology, the Exablate Neuro, has now treated thousands of people in more than 10 countries, including Canada, which approved it for treatment resistant essential tremor in July 2016.

When used for therapy delivery, FUS is paired with microbubbles to open the blood brain barrier safely and reversibly, thereby enabling therapies to slip through. This was once called impossible, owing to the blood brain barrier, which blocks entry of 98% of small and 100% of large molecules. World first clinical trials at Sunnybrook are proving otherwise, showing that FUS can breach the barrier and target amyloid plaque in Alzheimer’s disease. Trials in ALS and glioblastoma have also shown that FUS is safe and feasible in these conditions, too. Scientists at SRI worked with the company behind Exablate Neuro to modify the device for the blood brain barrier opening trials.
During treatment with the next-gen focused ultrasound device, a patient dons a customized brain device printed to their exact specifications. Next, thousands of beams of ultrasound are steered electronically to a target area, like a brain tumour. Microbubbles, tiny harmless gas bubbles that have been injected into the patient, interact with the sound waves, causing the blood-brain barrier to open temporarily. The therapy being delivered can then easily slip through the barrier and into the brain, directly to the area being treated.

As impressive as this is, it is the technology of Next-Gen Focused Ultrasound that will change medicine forever. It surmounts major limitations of the original unit. Frameless, it can steer the beams electronically to any area on the head.

Each patient will receive a customized device, built to spec, for personal treatment. Moreover, the device is being engineered so that it will not require pairing with MRI to monitor tissue damage, which will radically reduce its cost and increase its portability. None of this is possible with the current technology.

The human impact of this work is colossal, given the platform technology’s applicability to all neurodegenerative, oncological and psychiatric conditions. Take Alzheimer’s disease: Among G20 countries, there are about 37 million people with dementia, a number set to explode to 59 million in 12 years and 99 million by 2050. Annual costs of dementia for G20 countries are $754 billion (U.S.), and rising. As with other brain diseases, there are promising therapies in development; the biggest block remains delivery into the brain.

A first-in-human trial of the device in brain cancer will launch in 2021. Results will inform how the device needs to be modified for clinical use, knowledge that will be used to produce the devices for multicentre trials.
About Sunnybrook Research Institute

Sunnybrook Research Institute (SRI) is the research enterprise of Sunnybrook Health Sciences Centre, a teaching hospital fully affiliated with the University of Toronto. Our main aims are to understand and prevent disease; and develop personalized and precise treatments that enhance and extend life.

WE ARE INVENTING THE FUTURE OF HEALTH CARE.

Our scientists are internationally recognized experts in biological sciences, physical sciences and evaluative clinical sciences. Their expertise is brought to bear on the highest-need clinical areas, taking discoveries from the lab through to the medical marketplace.

**Specialized Centres and Multi-Institutional Projects**

Sunnybrook Research Institute has built specialized research centres and labs in partnership with the federal and provincial governments. Investment in these tops $200 million.

Our scientists lead large, multi-institutional projects in collaboration with the province and private sector, with a total budget of more than $30 million.

**International Presence and Partnerships**

Sunnybrook has the sole Centre of Excellence in Focused Ultrasound in Canada, one of only seven worldwide. We have the largest and most comprehensive focused ultrasound research program anywhere, with technical, preclinical and clinical expertise.

Sunnybrook Research Institute is a partner in Exactis, a pan-Canadian 11-member network that provides patients with accelerated access to clinical trials for precision cancer therapies. We are a lead molecular profiling site in the network, owing to our specialized capabilities in genomics sequencing.

We work with more than 90 companies to bring discoveries to patients.

We are a founding member of a global network to optimize the Elekta Unity, an image-guided radiotherapy system (MR-linac) developed by Elekta, a medical device company. We are the only centre in Canada with the system, and the lead for clinical trials of cancers of the brain and spine.

Sunnybrook Research Institute is a founding partner in the Heart and Stroke Foundation Canadian Partnership for Stroke Recovery, the first research organization in the world dedicated exclusively to stroke recovery.
Develop, Discover, Commercialize is produced by the Office of the Vice President, Research, Sunnybrook Health Sciences Centre and Sunnybrook Research Institute.

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DESIGNER: Clear Space Design
ILLUSTRATOR: Hang Yu Lin
PRINTER: Exodus Graphics

SPECIAL THANKS TO:
Dr. David Andrews and Jarkko Ylanko;
Dr. Greg Czarnota and Lakshmanan Sannachi;
and Alisa Kim and Matthew Pariselli.

ON THE COVER:
T cells (smaller round cells) attached to a cancer cell. T cells are a type of white blood cell that are important for keeping the immune system healthy, including protected from cancer. Engineering patients’ own T cells to fight cancer and other diseases is a promising new therapeutic approach. This picture was taken with a coloured scanning electron micrograph by Steve Gschmeissner / Science Photo Library.

250,000
square feet of research space, including the world’s first Centre for Research in Image-Guided Therapeutics

$109M
research funding in 2018–2019

1,171
publications in 2017–2018

2,108
citations of SRI publications in 2017–2018

323
scientists and clinician-scientists

445
active clinical trials

1,353
total research staff, including scientists, highly skilled personnel, and postdoctoral fellows and other trainees

SRI researchers hold Canada Research Chairs