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Executive Summary

Genome British Columbia (Genome BC) has committed to advancing the clinical implementation of precision health in BC in partnership with federal and provincial governments, research institutions, and the private sector. Precision health approaches adapt medical care for a patient based on their lifestyle, environment, and genomics. These initiatives rely on information about how the genetic sequence, or genome, of an individual influences everything from their risk of developing certain diseases to their likelihood of experiencing adverse drug reactions. There are now many examples of clinical applications of genomics including testing for rare diseases and cancer treatment – efforts supported by Genome BC. We look to add to these examples by supporting new opportunities where applied genomics research can effect transformational change in health care.

Traditional health care is at a transition point, with patients becoming more aware of the role genomics plays in their health and with rapidly evolving national and international efforts towards developing precision health initiatives. Genome BC is ready to be a leader in these efforts, coupling our existing programs with new strategies to address the roadblocks that slow the adoption of precision health as a standard of care in clinical settings. Through consultations, Genome BC has identified gaps and barriers in the health care ecosystem in BC that are limiting the clinical uptake of genomics research. Four cross-cutting themes emerged (education, big data, capacity and access) where coordinated effort is needed in order to advance clinical implementation of genomics in BC.

Leveraging our extensive knowledge of the BC scientific community, Genome BC will engage local stakeholders in research, health care, and policy to utilize proven genomic technologies in studies focused within the four cross-cutting themes. Well designed pilot projects in an area with clear potential for transformational impact will demonstrate solutions to these existing barriers. One such area with high potential is pharmacogenomics. Pharmacogenomics refers to the practice of assessing an individual’s genomics profile to understand how they will metabolize or react to a drug. Personalization of drug treatment plans can improve patient outcomes and reduce the economic burden that lack of efficacy and adverse drug reactions place on the BC health care system. This type of work will not only demonstrate the impact that pharmacogenomic testing could have if widely adopted in the BC health sector but, also showcase Genome BC’s role as a convener and facilitator.

Genome BC’s multi-pronged approach to the development and application of genomics research and application in BC has led to the recognition of Genome BC as a credible and trusted partner. Our investments help foster a world class genome sciences ecosystem, empower innovative entrepreneurs, educate the next generation, identify and address societal needs, and propel economic and social benefits for the province, Canada, and the larger global community. This document aims to:

- Share our vision of precision health with our partners and stakeholders
- Highlight the potential benefits of genomics in health care in BC
- Propose an expanded role for Genome BC as a facilitator to incorporate ongoing genomics innovations into the provincial health care system
1 The Role of Genomics in Precision Health

Genomics is the science that aims to decipher and understand the entire genetic information of an organism (such as humans and microorganisms) encoded in DNA and corresponding complements such as RNA, proteins and metabolites. This broad definition incorporates related disciplines such as bioinformatics, epigenomics, metabolomics, pharmacogenomics, proteomics and transcriptomics. These disciplines serve to associate biochemical information, like modifications to DNA and the presence of certain small molecules or proteins, to visible and tangible outcomes, like a physical trait or the occurrence of a disease. An interdisciplinary approach to genomics offers researchers in academia and industry a way to see the big picture of complex biological systems.

1.1 Path to Today

The Human Genome Project (HGP), a publicly funded international effort to sequence the entire human genome, empowered a movement that continues to revolutionize several industry segments including health care, agriculture, forestry, and energy. The original draft human genome, generated in 1999-2000, cost approximately $300 million to develop; according to an NIH report in 2016, the cost for a similar draft had dropped to less than $1,500. Similarly, the cost of accessing genomic sequence data is decreasing at an annual rate of approximately 30%. The returns from the development of genomics technology in general have been clear: the 2011 Battelle Report estimated a return on investment of 141:1 for the Human Genome Project in the US, with an initial investment of $3.8 billion yielding an economic impact of $796 billion. This boom in affordability, accessibility, and economic impact in the two decades since the completion of the HGP has been driven by the convergence of knowledge from fields such as life sciences, engineering, information technology and new materials.

This innovation has also raised the expectation of concrete clinical applications and better returns on investments and encouraged commercialization of genomics enabled technologies. In recent years, several entrepreneurial ventures, including Direct-to-Consumer genetic testing, have begun to utilize applied genomics to address gaps in “traditional” health care. This has served both to highlight the areas where health care is falling short and to demonstrate that patients are ready for wider action to modernize our approach to health care.
1.2 New Trends in Genomics Investments

Current global trends in genomics funding seem to be gravitating towards applied and translational precision health initiatives. In 2012, the UK announced a 100,000 Genomes Project that aimed to leverage genomics data to improve health care delivery and empower predictive, preventive, personalized, and participatory medicine (P4 medicine)\(^6\).\(^7\). This initiative, which was completed in 2018, led to a rare disease diagnosis for one in four participating patients and laid the foundation for the new Genomic Medicine Service from the National Health Service\(^8\). In 2015, France also announced their 10 year transformative plan, which was built around strong sequencing platforms, a national data analysis center, and a national reference center for technological innovation and transfer. With the goal of sequencing 235,000 genomes per year by 2020, France plans to utilize the resulting data to better anticipate and respond to health care needs in both primary care and acute settings\(^9\). Over the last two decades, recognizing the rapid pace of genomic advancements, Genome BC has allocated progressively more resources towards applied and translational projects with industry, government, and other user partners, creating a strong foundation for precision health initiatives with clinical and economic potential. This foundation has already resulted in tangible advancement of clinical implementation of genomics in a disease-oriented health care system, particularly in areas such as cancer, rare diseases, and infectious diseases.

![Diagram of Genome BC funding allocation across four consecutive five year strategic plans.](image)

### 1.3 Promise of Genomics in the Health Care Sector

Genomics has the potential to facilitate a shift from a largely disease-oriented health care system to one that is more proactive and less reactive. As genomics enabled technologies advance, we are no longer asking ‘if’ genomics should be integrated with clinical care. Instead we are asking ‘when’ and ‘how’ we can use genomics to benefit as many people as possible, across the entire health care continuum. Health care providers can rely on patients’ “omics” profiles to empower precision health efforts in both acute and primary care and for both population level public health initiatives and targeted individual treatment. Integration of genomics into the health care system leads to improvements in:
**Prevention: predict and prevent illness**

Understanding the nuanced differences between individual genomes (including, by extension, their proteome, metabolome, etc.) will allow us to better take advantage of the available data and tailor health care to the needs of a person rather than “an average” member of the population. Accounting for individuals’ variations could allow for personalized risk assessment of diseases in early life stages (cancer, diabetes, heart disease and asthma) and improve preventative efforts through targeted interventions.

Precision health care can consider not only our individual genomic profile, but also our lifestyle choices and familial history, all of which contribute to our overall personal health. Programs like the Genome BC supported Centre for Clinical Genomics (CCG) are already realizing the potential of capturing a more complete picture of a patient, including their hereditary and novel genomic risk factors. The CCG’s 17-gene Hereditary Cancer Panel, coupled with genetic counselling services, helps patients with a family history of cancer receive personalized screening recommendations for monitoring and preventative care.

**Diagnosis: develop disease profiles**

Genome sequencing can be used not only to understand the individual genomic variation in a patient but also the genomic variation unique to diseases like cancer. On the primary care side of cancer diagnosis, invasive diagnostic tests like biopsies can sometimes be replaced by economical single or multi “omics” profiling technologies, usually from a blood sample. This profiling also serves to provide critical information about the unique molecular profile of a tumor that can allow practitioners to go beyond identifying the tissue affected by cancer (e.g. prostate, breast) and into treatment customized to a specific tumor. Integrating genomics into diagnosis can also help differentiate between types of other complex diseases such as diabetes and facilitate early diagnosis of chronic diseases like asthma.

Disease profiles can also serve to guide treatment plans. Genome BC funded work is incorporating genomics based clinical tests into the management of cancer relapse to guide decision making for physicians and patients. Treatment plans can also be guided by the genomic profile of the patient.

**Treatment: create precision treatment plans**

A patient’s genomic profile can affect their response to medication and their likelihood of developing adverse drug reactions (ADRs). An adverse drug reaction is a harmful unintended consequence of a drug that has been properly administered at the correct recommended dose, usually prescribed by a medical
professional. Some ADRs are a byproduct of our genetic variations, which may affect our ability to metabolize drugs. It is estimated that there are approximately 200,000 severe ADRs in Canada each year, contributing to as many as 22,000 fatalities13. Overall health care expenses associated with ADRs in Canada are estimated to be upwards of $13 billion annually.

Pharmacogenomics, with its focus on using genomics to develop drug metabolism profiles, can help predict the effectiveness of medications, inform dosage, and reduce adverse drug reactions for everything from blood thinners14 to cancer medications11 (Appendix 1, 272PGX).

As personalized, targeted treatments prove more effective (with fewer side effects), patients’ adherence to treatment plans will also likely increase, improving outcomes and encouraging patient involvement.

**Participation: facilitate meaningful patient involvement in care**

Though action taken based on genetic data requires the participation of knowledgeable clinicians, the growing role of patients in the acquisition and use of genomic and other health related data will be an important and beneficial element of the precision health landscape. While it is impossible to predict where this increased patient participation will lead, it is also clear that stakeholders must support increasing patient participation in their own care. Genome BC is already increasing its involvement in this space with the GenCOUNSEL project, bringing together experts in genetic counselling, genomics, ethics, health services implementation and health economics to develop a framework for genetic counselling and patient involvement and service (Appendix 1, 276OGC).

### 1.4 Moving BC Towards a Precision Health Model

Genome BC, working with its research, industry, and government partners, is committed to realizing the full promise of precision health in BC. Our vision is that every patient and every individual in BC experiences benefits from genomic technologies. Our short-term mission stems from the knowledge that we must apply this vision to support the implementation of genomic-enabled technologies in the health care system.

Genome BC’s short-term mission in health is to:

- a. Work to unite the province around a common vision: one that puts genomics into action for precision health in BC
- b. Continue to support opportunities where genomics application can affect both incremental change such as in areas of oncology, rare diseases, and other specialized care – and transformational change as with the use of pharmacogenomics tests in primary care
- c. Work with key partners in BC to address the barriers and gaps that are slowing down the use of genomics in the health care system
- d. Understand the key opportunities for a rapid, cost effective, and socially responsible adoption of genomics and precision health in BC
2 The Potential for Socioeconomic Benefits in BC

Realizing the full potential of precision health requires a comprehensive understanding of not only the current economic and social challenges specific to the health care system in BC but also the potential economic benefits derived from increased uptake of precision health approaches.

2.1 Major Challenges Facing Health Care in BC

Increasing health care spending

A recent report by BC’s Auditor General shows that in the 2015-2016 fiscal year, BC spent $19.2 billion, or 41% of total provincial expenses, on health care. These numbers are a snapshot of a trend in rising costs: between 2012 and 2018, health care expenses are projected to increase by $2.7 billion \(^\text{15}\). This increase is more than the combined budgets of the 11 smallest ministries or even the entire budget of the third largest ministry (education). In the future, continued increases in health care expenditures could make it difficult for the provincial government to meet its spending and societal obligations.

Aging population with complex prescription drug needs

Data from BC’s Medical Services Plan (MSP) suggest that approximately 18% of the province’s 4.8 million residents are over the age of 65 and this percentage is expected to grow to 21% by 2025 \(^\text{16}\). This older population consists of significantly higher proportions of patients who are living with illness and chronic conditions (75% compared to 40.2% in general population) and are considerably more likely to take prescription medications (80% compared to 30% average for general population) \(^\text{16}\). These older patients are twice more likely than the general population to take multiple prescription medications \(^\text{17}\), also increasing their risk of ADRs. These drug reactions create a high financial burden on the Canadian health care system. It has been reported that up to one-quarter of patients who visit emergency departments due to ADRs are admitted to hospital\(^\text{18,19}\). One recent study found that emergency room visits and hospital admissions due to ADRs among seniors in Canada cost an estimated $35.7 million, with more than 80% of those costs arising from hospitalization\(^\text{26}\). Moreover, ADRs resulting in hospital admission generally represent more severe reactions and often require more resources to treat\(^\text{25,20}\). An aging population with high prevalence of chronic disease, in BC and the rest of Canada, is a clear target demographic that would benefit from effective translation of research about the genomic underpinnings of ADRs into clinical recommendations.

Disparities in access to care across BC

BC’s size and varying population density contribute to an uneven distribution of resources. Highly dense urban areas like Vancouver benefit from centralized community health centres, specialized care, and hospitals, while more remote regions have more limited, decentralized access to some resources including genomics technologies. Cultural views of Western medicine can also affect the utilization of services by certain populations, adding to the disparity of access. The Silent Genomes project, funded by Genome BC, seeks to initiate preliminary conversations with individuals of Indigenous ancestries to determine their perspectives, values, and concerns while raising awareness of under-representation in
genomics databases (Appendix 1, 275SIL). Projects like this exemplify how the careful development of new partnerships can help previously underrepresented patient populations get improved access to the level of personalized data that has the potential to improve their standard of care.

2.2 Economic Benefits of Genomics and Personalized Health

For any new technologies such as genomics, there must be a clear health economic analysis and a business case to ensure a sustainable contribution to health care. In personalized health, the returns on investment are already apparent, with benefits to patients and significant economic returns.

**Rapidly growing market:**

Non-government investments in precision health have increased significantly, leading to considerable growth in the number of personalized therapeutics. Between 2005 to 2016, there has been a dramatic increase in the number of genomics enabled drugs on the market, from five to 132. In 2016, personalized medicines that identify specific biomarkers accounted for 27% of all molecular entities approved by the Food and Drug Administration (FDA), compared to only 5% in 2005. A survey by Tufts Center for the Study of Drug Development estimates that 42% of all drugs and 73% of oncology drugs in development during 2015 utilized a biomarker and have the potential to be personalized.

**Innovations in diagnostics:**

Within the larger context of the global personalized medicine market, drugs reliant on companion diagnostics are a leader. Companion diagnostic tests evaluate whether a patient is a suitable candidate for a particular drug based on the presence of genetic or other key biomarkers. Use of these diagnostic tests facilitates a personalized medicine approach and is a growing component of cancer and complex diseases treatment. Companies offering diagnostic tests were responsible for revenues of $25B in 2015, which is expected to grow significantly in the next five years. The majority of these tests are designed to facilitate appropriate therapy selection for oncology.

**Reduced public health costs:**

Beyond generating revenue through the growth of a new market in genomics enabled drugs, precision health has the long-term potential to reduce the burden on the public health system through preventative care. Tangible economic benefits come from early detection and prediction of infectious disease outbreaks and regular screening of patients with high hereditary risk of cancer. A 2017 report from the World Health Organization suggests that cancer treatment regimens for patients diagnosed early cost two to four times less than later stage treatment. Similarly, a detailed analysis of the projected...
economic impact of improved early cancer diagnosis in England estimates an annual savings of £210 million (CDN $350 million) for their health care system. Beyond the improved prognosis for patients, there is a clear economic case for using the tools at our disposal, like genotyping, to improve screening programs.

Despite the clear benefits of applying genomics to precision health initiatives, there are still significant barriers to the adoption of precision health approaches as a standard of care in clinical settings.

3 Addressing Barriers to the Clinical Implementation of Genomics

In consultation with diverse BC stakeholders, Genome BC has identified four cross-cutting areas serving as barriers to the uptake of genomics in health care: education, big data, capacity, and access. These areas are consistent with barriers that have been observed elsewhere, but have challenges and opportunities specific to BC. Using our position as a capacity builder within the larger BC scientific community, we have already begun to develop efforts to overcome these limitations and propose that with an active role as a facilitator Genome BC is a powerful partner to move genomics innovations into clinical practice.
3.1 Barriers to Implementation

**Education**

With the rapid pace of new discoveries in genomics, staying up-to-date poses a challenge even for experts. The UK’s experience with the 100,000 Genomes Project has highlighted the need for dedicated resources to educate not just the doctors but also the patients receiving care and the health care providers involved in delivering precision health care. Genome BC recognizes the need in our health care sector for providing formal and informal training to health care providers involved in the patient journey to ensure they understand the benefits genomic data can provide their patients. We are well positioned to facilitate the development of tools to support health care providers in their daily practice, to demonstrate the role that genomics plays in their health and daily life and to engage in outreach efforts that highlight the promise of precision health care while being socially responsible and managing expectations.

Efforts are already underway at Genome BC to integrate genomics education across multiple channels, from secondary school education (Geneskool™) to public science forums (GeneTalks). Our popular Geneskool program, active across BC since 2006, provides resources for teachers and programs for students in grades 9-12, including classroom workshops, field trip opportunities, travelling exhibits, free classroom resources, and a summer science program. We act to bring together the many groups involved in delivering education to identify the current status of and potential gaps in genomics education in BC, and to assess future needs in a rapidly evolving ecosystem. Genome BC is planning to use our experience with these programs to address gaps in the education of health care providers on the use and benefits of genomics in the context of precision health.

**Big Data**

Genomics related disciplines generate an enormous amount of data which are challenging to integrate, aggregate, harmonize, and share. Data often sit in silos, stored within the confines of research institutions and laboratories. This approach to data storage restricts the centralization and interconnectivity that makes crucial data accessible to the larger research and clinical communities. Efficient methods of data storage, processing and analysis can enable the connection of data sets which
improve the interpretation of research outcomes and help integrate research data with clinical data. At the provincial, national, and international level, discussions are underway to generate standards and quality assessments for data generation, formatting, storage and consent with the intent to facilitate the sharing of data for the benefit of end users i.e. patients and their caregivers. Well defined solutions should be delineated and actions prioritized.

Genome BC is positioned to help lead this process and broker governance and policy support to ensure effective, secure and appropriate use of data. We are engaged with the Global Alliance for Genomics & Health, which focuses on challenges in data sharing policies and standards, and with Canada’s Digital Technology Supercluster, which aims to identify opportunities and support initiatives that may provide solutions to these challenges.

**Capacity**

Developing the infrastructure needed to enable the broad application of genomics technology also warrants extensive consideration. Such infrastructure includes data, biobanks, sequencing infrastructure, assay development, decision making tools, and highly qualified personnel (HQP) to interpret research findings and incorporate into the standard delivery of care. It is also important to consider how the infrastructure can be easily mobilized, particularly in regions that may lack the required HQP (genetic counsellors, bioinformaticians, etc.). Key stakeholders in BC should capitalize on this timely opportunity to envision the dissemination of genomic test results depending upon complexity: for example, centralizing cutting edge technologies requiring specialized equipment and personnel while decentralizing services for more straightforward multi-gene panels and single-gene tests across the province.

Building capacity is at the core of our mission at Genome BC. With our investments, Genome BC has consistently helped promote and cultivate strong research teams and state-of-the-art platforms. With our project development resources, we have helped BC scientists develop high quality research proposals and consistently secure federal funding investments that strengthen our genomics research and applications ecosystem in BC.

**Access**

Successful implementation of precision health care in our province should be predicated on harmonization of delivery mechanisms of genomic/genetic information such as policy development and economic evaluations. Currently, informed consent and ethics approval pipelines between research institutions and hospitals are varied and uncoordinated. There is additional need for streamlining the evaluation and cost-benefit analysis process for genomics-derived tools that have the potential for adoption within a publicly funded health care system. There is an opportunity now for information to be aggregated from counterpart Ministries and service providers across Canada to avoid the duplication of Pan-Canadian efforts; this would make it easier to assess the economic feasibility of genomic applications in health care. There must be a well articulated business case behind the cost of new treatments and procedures to ensure that precision health, as a clinical standard, will contribute to the long-term sustainability of the health care system. On this front, Genome BC and Genome Canada have
made a conscious effort to ensure that health economic studies are embedded in large scale funding proposals and that social, ethical and legal aspects are considered when necessary.

Patient privacy is also at the forefront of discussions about access. Insights from other jurisdictions as well as from private service providers highlight patients’ concerns regarding ownership, sharing and privacy of their data. Advances in precision health care and machine learning can significantly increase our predictive abilities, with implications even for those not directly involved. It is crucial to engage with the BC Privacy Commissioner early on in this process regarding issues such as genetic discrimination and the legal framework supporting genetic privacy and freedom under the Genetic Non-Discrimination Act. Guiding principles for a legal framework would include validated scientific data and a comparison of current methodology to inform recommendations and guidelines put forth by clinical task forces. Policy makers are challenged to establish practical regulations that limit the most controversial practices, while ensuring genomic applications are benefiting society, and connections to the scientific community through an established organization such as Genome BC could serve as a valuable resource.

Genome BC aspires to be the change agent that will assist the health system in the adoption of precision health. Beyond the role of research funder, Genome BC can play the role of convener, bringing together diverse stakeholder groups to encourage the collaborative efforts necessary to make changes that can impact the existing health system. We have designed a pilot initiative focused on pharmacogenomics, a clear area of need, to demonstrate the positive impact that genomics can have on the development of a modern, innovative, and cost-effective health care system.

3.2 From Incremental to Transformational Change

Genomics enabled technologies have already been shown to improve health outcomes in specific patient populations. Recent projects within Genome BC’s own portfolio include: sequencing relapsed lymphoid cancers to identify biomarkers that might improve patient outcomes; using genomic analysis of stool samples to identify microbial populations missing in infants who later develop asthma; using genomics tools to reduce the risk of kidney transplant rejection (Appendix 1, 273AMR) and many more. Despite the growing application of genomics, especially in oncology and rare diseases, implementation in the health care system is incremental, focusing mainly on hospital and specialized care. We see an opportunity for a pilot initiative to further enable opportunities for genomics driven transformational change in health care not just for specific patient populations in a hospital context, but for all patients at the point of primary care.
Working with our partners, Genome BC has identified pharmacogenomics as one area that shows early potential for affecting transformational change to the health care system, moving towards a preventative rather than reactive approach and actively addressing the crosscutting themes we identified. Clinical use of pharmacogenomics has already shown great promise, yet it is not widely adopted in the public system. Key stakeholders have already been contributing to the momentum for integration of pharmacogenomics in our health care ecosystem in a responsible and evidence-based manner to ensure maximum benefits for patients and best utilization of our health care budget. Pharmacogenomics is poised to serve as an example of the impact genomics enabled technology can have when applied for preventative care.

I. Pilot objectives and scope

The goal of our current pilot initiative is to facilitate new projects and inclusive stakeholder involvement to develop the pharmacogenomics sector in BC. To minimize the risks associated with the inherent complexity of such projects, with diverse patient populations and a variety of stakeholders, we will focus on proven genomic applications. Managing complex projects with partners has long been a core competency for Genome BC. To identify alignment and clarify responsibilities we plan to leverage our expertise to engage with potential stakeholders including our academic partners, industry collaborators, health care providers (such as physicians, nurses, pharmacists, and genetic counsellors), the BC Ministry of Health and other funding partners.

II. Pharmacogenomics offers great promise with proven effectiveness

Pharmacogenomics applications have already proven effective in increasing drug efficacy and reducing drug events, key priorities for BC and Canada. Currently, providers from Canada and around the globe such as myDNA, Dynacare, GenXys, Molecular You, and 23andMe offer pharmacogenomics-related applications to BC residents; the opportunity to build on existing infrastructure supports the appeal of this pilot initiative. Some providers such as myDNA and GenXys have established local partnerships (with the BC Pharmacy Association and LifeLabs, respectively) with health care providers to encourage guided results analysis. Other providers have, to this point, mainly focused on direct interactions with consumers. Regardless of the approach, advances made by these platforms provide validation for the growth of genomic technologies and stoke patient interest in pharmacogenomics. Now is the time to meaningfully engage with health care professionals to ensure high fidelity of diagnosis and treatment is attained.

III. Broad partner engagement is essential

In BC, General Practitioners (GPs) act as gatekeepers of primary care. GPs in BC are often private business owners with busy schedules and high patient loads. Pharmacogenomic testing may be well suited for involving other health care providers, including nurses, pharmacists, and genetic counsellors, helping alleviate some of the burden on GPs. It will be important to engage with all of these providers to understand the best ways to implement a new technology that will face inevitable challenges involving data sharing and interconnectivity of systems. This would also open the door to future involvement for all practitioners in later genomics applications.
Application of pharmacogenomics has the potential to affect transformational growth of genomic technologies in health care. As an inaugural pilot, it relies on proven technologies with various implementation avenues and immense potential for system gains. With targeted development of precision health initiatives, BC could position itself as a national and global leader in developing recommendations and guidelines for genomics as a clinical standard in health care. Genome BC is the right partner for bringing together the cross-sector stakeholders (including the Ministry of Health, health authorities, international experts and health care providers) who are crucial to addressing barriers to precision health uptake in the BC health care system.

4 Genome BC as a Key Partner

Since its inception in 2000, Genome BC has led genomics innovation on Canada’s West Coast and continues to facilitate the uptake of genomics for social and economic benefit. We invest in research, entrepreneurship, and commercialization to maximize health benefits of innovative genomic solutions for all patients. Projects supported by Genome BC and its partners have already begun to show the promise of genomics applications in health care. We have successfully worked with provincial and federal governments as well as public and private organizations to support world class genomics research projects (discovery, applied, and translational), invest in technology development and platforms, and promote strategic partnerships.

Investing in the BC economy

We have managed a cumulative portfolio of over $1 billion in more than 390 genomics research projects as well as science and technology platforms. Based on a recent report, our efforts have impacted BC’s GDP by $2.6B and attracted $805M in co-investments. During this time, we have partnered with 979 groups, created and enabled 32,400 jobs, advanced 86 companies and supported 660 patents. Within the health sector specifically, we have catalyzed and managed 206 projects representing an investment of $504M. It is important to note that genomic investments have long maturity dates and many of those considered in our analysis may not have yielded their full impact. These factors have helped foster global recognition of BC’s scientific strength in genomics and related technologies.

Fostering a world class genome sciences ecosystem

The result of these investments is not just economic benefits, but also the establishment of Genome BC as a trusted independent partner providing insights and advice to governments, researchers, the private sector and the public. This unique position combined with a carefully crafted strategy prioritizing end user needs, has enabled
Genome BC to cultivate a world class genomics hub in our province. To ensure continued success we rely on our competitive advantage:

- Identification of high priority, impactful projects
- Funding & program management
- Supporting cross-sector relationships
- Analysis of project based social and economic benefits
- Addressing societal issues early in the application of genomics

In this regard, the projects supported through the 2017 Large-Scale Applied Research Project (LSARP) Competition in Genomics and Precision Health align well with our mission. Brief descriptions of these projects can be found in Appendix 1.

**Incorporating societal impacts into research translation**

Genome BC has also taken a leadership role in exploring the societal aspects of genomics research. The rapid advancement of genomics and its uptake both locally and globally, will undoubtedly raise concerns; not only over how advancements may impact our lives, but also how these technologies can benefit society through their application. To promote economic and social benefits, we utilize multiple approaches, from education and outreach programs, to focused funding opportunities and user partnerships. Through collaborations with government, academia and industry, Genome BC continues to translate the excellent research carried out in universities into applications that will ultimately benefit not only BC and Canada, but health systems globally.

Progression from research, to validation, to pilot and large scale clinical implementation requires support and guidance from experienced partners. Genome BC is ideally situated in the BC scientific community to serve as that partner and facilitate productive new collaborations and research initiatives. Our goal is to support genomics enabled solutions for specific target areas in BC where clinical utilization and the benefits of genomics can be demonstrated.

### 5 Conclusion

Genome BC, in partnership with federal and provincial governments, research institutions, and the private sector has committed to support and advance precision health in BC. Our investments to date have helped drive economic and social benefits to the province, Canada, and globally. Our goal is to encourage the utilization of genomics as the standard in clinical care, in areas where it has the potential for positive impact. In this regard, we continue to support areas where genomics can impact patient care such as oncology and rare diseases. However, we also believe it is time for us to seize opportunities where genomics can affect transformational change in the health care system. Pharmacogenomics offers a prime prospect for BC. There is great potential for pharmacogenomics and other genomics applications to improve disease prevention and treatment. Genome BC is well positioned to develop collaborative pilot initiatives to identify practical solutions to the barriers that hinder adoption of precision health in clinical care.
Appendix 1: Examples of Large-Scale Applied Research Projects

Silent Genomes – Reducing Health Care Disparities and Improving Diagnostic Success for Children with Genetic Diseases from Indigenous Populations (275SIL):

First Nations, Inuit and Métis’ populations, collectively known as the Indigenous Peoples’ of Canada, face strikingly similar health challenges with global Indigenous Peoples’. Inequities include barriers to health care access that produce poorer health outcomes compared to non-Indigenous groups.

Whereas genomic technologies are advancing health care by allowing medical treatments to be tailored to the specific needs of individual patients (precision medicine), this “genomics revolution” is widening the health inequities gap. In particular, compared to what is becoming routinely available to other Canadians, Indigenous populations often have little or no access to genomic technologies and the research that drives them, hence intensifying the “genomic divide”.

A key concern in the growing genomic divide is the lack of background genetic variation data for Indigenous populations living in Canada and globally. This prevents accurate diagnosis because the reference data are needed for precise genetic diagnosis. Notably, standard genomics resources are silent with respect to First Nations (FN), Inuit and Métis. Silent Genomes will address the genomic divide by reducing access barriers to diagnosis of genetic disease in Indigenous children.

Silent Genomes, is a game changing partnership with First Nations, Inuit and Métis Peoples that will:

- establish processes for Indigenous governance of biological samples and genome data,
- lead to policy guidelines and best practice models, bringing equitable genomic testing to Indigenous children in Canada with suspected genetic diagnosis, and
- develop an Indigenous Background Variant Library (IBVL) of genetic variation from a diverse group of First Nations in Canada.

Silent Genomes will improve health outcomes by enhancing equitable access to diagnosis, treatment, and care while assessing cost effectiveness of precision medicine.

Deciphering the Genome Biology of Relapsed Lymphoid Cancers to Improve Patient Management (271LYM):

Lymphoid cancers, which start in the immune system and include Hodgkin’s and non-Hodgkin’s lymphoma, myeloma, lymphocytic, and lymphoblastic leukemia, are the fifth most common cancers in both men and women and affect people of all ages. Every year in Canada, 16,000 people are diagnosed with a lymphoid cancer and for 6,000 of them, it is fatal. Death most often occurs when disease relapses after an initially successful treatment, making treating and controlling the symptoms of relapsed disease the most pressing need for patients suffering from lymphoid cancers.

Because the causes of relapse are not known, and because relapsed cancer differs considerably from the initial cancer, there are no clinical tests to provide information on the prognosis for individual patients and likely treatment outcomes, or to provide guidance to physicians and patients on the use of alternative...
therapies, such as small molecule drugs or immunotherapy. Relapses and associated treatments cost the Canadian health care system more than $315 million each year, about 10 per cent of the expected cancer drug budget in 2022, and the lack of clinical tests means many of these expensive treatments are applied without adequate guidance.

Drs. Christian Steidl, Marco Marra and David Scott of the BCRC are developing genomics based clinical tests to improve patient outcomes and quality of life, and working to integrate the tests in the health care system. To do so, they will sequence relapsed tumours to identify novel biomarkers. They will undertake economic analyses to better understand the cost effectiveness and health system impact of genomics informed management of relapsed disease. They will also develop an e-health application to assist patients with shared decision making.

The results of this project will be novel clinical tests that will provide decision aids for physicians and patients, assist policy makers in the implementation of personalized treatment approaches for relapsed lymphoid cancers and reduce the costs of treating relapsed lymphoid cancers.

**Childhood Asthma and the Microbiome – Precision Health for Life: The Canadian Health Infant Longitudinal Development (CHILD) Study (274CHI):**

Asthma is the most common chronic disease of childhood, affecting one in seven Canadian children (and more than three million Canadians of all ages). It is the most common reason for children to be admitted to hospital and to be absent from school. It is also expensive, costing more than $2 billion per year in Canada. Treatments can manage symptoms, but there is no cure, only the hope that children will “grow out of it.”

Dr. Stuart Turvey, his team at the University of British Columbia and the CHILD study team are focusing on early diagnosis and prevention, two factors that can reduce the personal and economic toll of asthma. Their sample of choice comes from dirty diapers: by using powerful genomics technologies to analyze stools, they may be able to predict which infants will go on to develop asthma. The reason? Evidence has shown that babies who go on to develop asthma tend to be missing key microbes in their intestines (the microbiome, as it is known) in the first few months of life. Beyond predicting who may develop asthma, thus enabling early diagnosis, the research will guide the ethical development of ways to replace these microbes, to prevent asthma from developing at all.

**Stages of microbial colonization of the infant and child intestine:**

GenCOUNSEL – Optimization of genetic counselling for clinical implementation of genome-wide sequencing (276OGC):

Genome-wide sequencing (GWS) is a powerful new genetic test that analyzes a person’s entire genetic make-up. While valuable, it can be problematic, by revealing disorders or disease risk factors unrelated to the original reason for testing, or by generating complex findings that are difficult for non-expert health providers to interpret. While not currently routinely available, genome-wide sequencing will soon be in more widespread use for patients who need it – increasing demand for genetic counselling, to which access is already limited in Canada.

Genetic counselors provide education and emotional and decisional support to patients and families, helping them to make informed decisions about genetic testing and its results. Because of lack of legal recognition of genetic counselors in Canada, most of them are found in academic centres rather than in the community.

GenCOUNSEL, which brings together experts in genetic counselling, genomics, ethics, health services implementation and health economics, is the first project to examine the genetic counselling issues associated with clinical implementation of GWS. It will determine the most efficient socioeconomic, clinical, legal and economic methods of providing genetic counselling once GWS is available in the clinic. It will create an understanding of current and future needs for genetic counselling, develop best practices for the delivery of genetic counselling, improve access to the counselling, particularly for underserved patient populations and develop a framework for the legal recognition of genetic counselors. The result will be increased access, patient satisfaction and cost efficiency while providing genetic counselling to all Canadians who need it.

Genomic and Outcomes Databank for Pharmacogenomic and Implementation Studies (Go-PGx) (272PGx):

Adverse drug reactions (ADRs) are a major problem in modern medicine, leading to withdrawal of treatment, non-compliance with medication, permanent disability and death. This is particularly true for cancer treatment, with its potent medications. The vision of Go-PGx is to save lives and improve the quality of life of children with cancer, by using genomics based precision health strategies to reduce the most common and serious ADRs in these children.

It is increasingly evident that genetic differences in patients can affect the likelihood of their developing an ADR. Drs. Bruce C. Carleton and Colin J. Ross, both of the University of British Columbia, are working to prevent these ADRs by developing lab tests to predict the likelihood of a childhood cancer patient developing an ADR and tools to incorporate these tests into clinical practice. Through Go-PGx, they will analyze more than 6,125 DNA samples and corresponding medication use and ADR outcome data to discover biomarkers that will reveal genetic susceptibility to ADRs and develop tools to educate and inform physicians and patients, beginning with five of the most severe ADRs in childhood cancer. They will also develop a comprehensive database linking clinical and genetic data as an accessible resource for researchers throughout the world. With the data they generate, they will begin providing testing at 10 pediatric cancer centres across Canada, while studying barriers and facilitators to the uptake of ADR screening in the health care system, as well as the economic implications of introducing this kind of
testing into clinical practice. The team will also develop peer reviewed clinical practice guidelines before project completion and publish them within a year post project.

**Precision Medicine CanPREVENT AMR – Applying Precision Medicine Technologies in Canada to Prevent Antibody Mediated Rejection and Premature Kidney Transplant Loss (273AMR):**

Transplantation is the treatment of choice for patients whose kidneys have failed, providing superior survival, better quality of life and lower health care system costs (<$20,000/year vs. > $90,000) compared with dialysis. However, a severe form of rejection (known as antibody-mediated rejection, or AMR) causes premature loss of the transplant kidney in as many as 30 per cent of transplant recipients, or 500 Canadians every year, prompting a return to dialysis and often early death.

The team led by Drs. Paul Keown and Stirling Bryan of the University of British Columbia, Ruth Sapir-Pichhadze of McGill University and Timothy Caulfield of the University of Alberta and includes an additional 70 scientists and clinicians from 22 universities in Canada, the US, the UK and the EU, will use genomic technologies to reduce the risk of AMR. These will enable better matching of patients and donors, precise monitoring of the immune response after transplantation to better predict AMR, and the use of personalized drug treatments to prevent rejection while avoiding infection or cancer. The team will also engage patients, providers and health care payers to study the legal, ethical, societal and economic considerations of introducing these strategies into clinical practice.

The goals of the research program are to reduce the frequency of AMR by at least 50 per cent and in so doing, first benefit the patient and his or her family through improved survival and quality of life, reduced caregiver burden and personal health costs; second to minimize demand on the health care system by reduced costs through decreasing dialysis and re-transplantation, and third to improve care of a major chronic disease by increasing productivity and streamlining the management of chronic kidney failure.

**Care4Rare Canada – Harnessing Multi-Omics to Deliver Innovative Diagnostic Care for Rare Genetic Diseases in Canada (277C4R):**

There are more than 7,000 rare diseases in Canada which have a devastating impact on more than one million Canadians and their families: two-thirds of these diseases cause significant disability; three-quarters affect children; more than half lead to early death; and, almost none has any treatment. Further, the cause of more than one-third of these diseases is not known. Building on the work of the Care4Rare Canada Consortium, the C4R-SOLVE project is working to identify the genetic cause of unsolved rare diseases and make genome-based clinical diagnostic tests available. These tests will speed up the diagnostic process, thereby preventing years of what can be a seemingly unending series of visits to specialists and testing – difficult for families and expensive to the health care system.

Key to C4R-SOLVE’s success will be new sequencing technologies and improved worldwide data sharing. In addition, the group will work with provincial ministries of health to determine how best to include genome sequencing as a clinical test to diagnose rare diseases, beginning with Alberta and Ontario. In doing so, C4R-SOLVE will more than double our ability to diagnose patients with the one-third of rare diseases whose cause is, at present, unknown, while building infrastructure and tools to improve diagnosis throughout the world. Accurate and early diagnosis will optimize care, improve the wellbeing of
patients and their families and provide new insights into these devastating diseases, while potentially saving at least $28 million/year in health care spending.

PEGASUS-2 – Personalized Genomics for Prenatal Abnormalities Screening Using Maternal Blood (278PEG):

The discovery that fetal DNA is present in the mother’s blood during pregnancy has led to the development of a genomics based maternal blood test called NIPS (non-invasive prenatal screening), which is a very reliable test for Down syndrome. In part due to its cost, NIPS is currently only used as a second-tier test, after a mother has tested positive on less costly and less accurate tests, to confirm the finding, without resorting to amniocentesis.

Making NIPS the entry-level test for Down syndrome would benefit women by more accurately detecting an affected pregnancy with less chance of a false positive result and by providing that result earlier in the pregnancy. As well, because NIPS can detect other chromosomal abnormalities, its use could enable screening for more conditions. The PEGASUS-2 project’s goal is to provide high quality evidence to support the use of NIPS instead of traditional screening tests by comparing its use as a first tier and second-tier test in a large cohort of pregnant women. The project will also study the cost effectiveness of expanding screening to other conditions and the ethical, social and legal implications of doing so. It will also provide strategies to promote shared decision making between couples and health care professionals. Finally, it will further develop the NIPS technology to reduce its costs by 50 per cent and expand its ability to detect other anomalies, as well as ensuring quality control for clinical NIPS testing in Canada and worldwide.

PEGAGUS-2 will enable publicly funded access to a promising genomics technology for all pregnant women, while ensuring that couples have access to web based tools to help their decision making and that all health care professionals are trained in shared decision making for prenatal screening.
Endnotes


2 Wetterstrand KA. DNA Sequencing Costs: Data from the NHGRI Genome Sequencing Program (GSP). Available at: www.genome.gov/sequencingcostsdata. Accessed on 1/7/18.


7 The 100,000 Genomes Project: bringing whole genome sequencing to the NHS. BMJ 2018;361:k1952 doi: https://doi.org/10.1136/bmj.k1952. 02 May 2018.


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