



RNA Canada ARN

EXECUTIVE SUMMARY

RNA: The new frontier

The central dogma of molecular biology explains the flow of biological information, where DNA is copied into RNA and RNA is used to make proteins.

Despite the fact that mRNA was discovered over 60 years ago, exploiting this paradigm for the benefit of the human condition has focused mostly on DNA and proteins.

On the DNA side, genomics has permitted identification of mutations that disrupt gene function, while genome-editing technologies have recently given scientists the ability to modify portions of an organism's genome to correct deficiencies.

On the protein side, altering protein functions with antibodies or with small molecules has led to striking advances in the fight against human diseases.

On the RNA side, tremendous progress had been made in understanding its roles and functions, but it was the **COVID pandemic** that allowed **RNA** to move to center stage and to demonstrate its potential as a **game-changing** and disruptive technology. This timing was historic, primed by a convergence of fundamental discoveries and maturing technologies that provided unique opportunities to exploit the extraordinary power of **RNA**, both as a **tool and** as a **target**.

As a **tool**, RNA vaccines have been designed to reprogram the functional output of animal or plant cells. RNA-based technologies are now being applied against a large variety of diseases and emerging threats. In addition to the **upcoming wave** of mRNA- and **antisense-based** approaches, the RNA-based CRISPR **gene editing** technology is also expected to revolutionize our ability to **improve** many aspects of **human health**.

Because RNA is remarkably versatile and performs multiple functions, from encoding every protein in the cell to regulating nearly every cellular process, **RNA** molecules **expand** the **repertoire of biological targets** available to alter cellular functions. Targeting RNA molecules with antisense oligonucleotides, with CRISPR-based technologies, or with new generations of small molecules is providing exquisite specificity in a large variety of innovative applications. One critical advantage of targeting **RNA** relative

to DNA is that this approach **leaves no trace** on the genome, thus mitigating concerns about transmissibility. Moreover, the hundreds of proteins that recognize, modify, or degrade RNA represent an additional untapped reservoir of biological targets and tools for biomedical, environmental, and agricultural applications.

The **outstanding potential of RNA-based technologies** and the diverse functional attributes of RNA molecules in biological processes therefore **warrant** using and targeting RNA in **strategies against future existential threats**, from **new pandemics** and non-communicable diseases **to** the impact of **climate change** on health, agriculture, and vital natural resources.

RNA Canada ARN

As a **not-for-profit organization**, RNA Canada ARN's mission is **to develop a concerted strategy** to discover, leverage and apply RNA-based discoveries with high impact and of tremendous **benefits to Canadians**. As we are only at the earliest stages of revealing the full disruptive potential of RNA-based innovation and discovery, supporting RNA science in a coordinated manner will not only accelerate the pace of fundamental discoveries but will be essential to the development of innovative and multidisciplinary strategies in health, agriculture, environment, and forestry, as well as to capture the associated socio-economic benefits for Canadians.

The philosophy of RNA Canada ARN is to work with existing funding agencies and existing large-scale initiatives to coordinate and not duplicate efforts. RNA Canada ARN will help interested partners and funding agencies identify the needs and opportunities of RNA research in Canada.

The socio-economic impact of RNA technology is growing exponentially and is expected to reach over **150 billion US dollars by 2026**. Already, the world is gearing up to this RNA revolution with many countries establishing special strategic programs in RNA science. With over 225 laboratories carrying out RNA research, Canada is recognized internationally for the quality and innovation of its RNA research. The **Canadian RNA ecosystem** is dynamic, interactive, and ideally suited to embark on a concerted effort to maximize the outcome **of innovative RNA technology**. The creation of **RNA Canada ARN** reflects the enthusiasm and the leadership of Canadian RNA research scientists in harnessing the power of RNA for the benefit of all Canadians.

Canada boasts a very dynamic life sciences and biotechnology sector with over \$54 billion in annual revenue in 2018. RNA-enabled technologies are becoming an integral part of this global national picture (for example, with **Moderna constructing its RNA vaccine manufacturing plant in Quebec**). Government agencies are also starting to recognize RNA as central in future efforts towards pandemic preparedness (for example, through the Canada Biomedical Research Fund program). On the other hand, while the federal **Tri-Council** framework currently **supports** RNA research through competitive peer-reviewed grant applications, this effort is **not tied to a national strategy** that would promote the development **of RNA science**. National **strategies** on RNA science are now being **designed in** different countries including **Australia, UK and Japan**.

RNA Canada ARN represents a comprehensive grass-roots consortium of national independent experts on RNA. It **was established** with the objective of providing an assessment of the gaps in our RNA-innovation ecosystem, suggesting pro-active solutions, and identifying emerging opportunities **to strengthen our national leadership** in RNA science. **RNA Canada ARN** aims to provide strategies and guidance to national funding agencies on all aspects of RNA science. **RNA Canada ARN aims to** improve and **coordinate** interactions among RNA scientists and stimulate partnerships between the **academic** and **industrial** sectors to help leverage Canadian RNA **expertise**. For this expansion of RNA science in multiple sectors to be beneficial to Canadians, it must be tightly tied to programs that educate and train a new generation of scientists and given the unprecedented speed of adoption across all sectors, provide reskilling opportunities in RNA science for existing science professionals and technologists. Finally, the RNA community must monitor the outcome of this effort and has a responsibility to educate all stakeholders in RNA biology with respect to societal impact and risks.

RNA Canada ARN's mission is to **transform** Canadian RNA **research into** an efficient, effective, flexible and competitive pipeline dedicated to RNA **discoveries** and their optimal use **for** the benefit of **all Canadians**.

RNA CANADA ARN's objectives are:

1) to promote the creation of an **investment program in RNA technologies** to stimulate innovation and the application of RNA discoveries. This investment **program** will be dedicated to financing four categories of projects.

- a. **Large-scale projects** led by RNA scientists in the academic sector that will be aimed at developing new technologies or adapting or expanding the usefulness of emerging or evolving technologies to specific areas. It is essential that **funding** of RNA research is **not limited to human health but** that it also includes key economic sectors such as **agriculture, aquaculture, environment, and forestry**, which are intimately tied to challenges in food security, climate change and biodiversity. Such large-scale **cross-sector projects** will ultimately **contribute to** Canada's **crisis preparedness** and increase **economic recovery** and resilience. Projects that integrate discoveries and tools initially developed for human medical applications could serve to implement new procedures in agriculture, environment, and forestry. Another example could be the **integration of artificial intelligence (AI)** in the forward-engineering of RNA tools and biological targets **for** the development of **new vaccines** and/or new **green technologies**. Our innovation ecosystem includes multiple players from various fields of expertise. Large-scale, multidisciplinary research projects are often triggered by interactions between basic researchers and practitioners from different sectors (AI, human and animal health, agri-food, etc.). Many opportunities are arising at the intersection of these sectors combining different expertise for the benefit of innovative projects. **RNA Canada ARN** therefore wishes to facilitate the funding of large-scale projects dedicated to exploring intersectorial endeavors.
- b. **RNA application projects** dedicated to translational applications and knowledge mobilization. **RNA Canada ARN's** objective is to become a one-stop shop for accessing RNA innovation capacity to develop and deploy RNA-enabled solutions for future pandemics,

human and animal diseases and other challenges such as crop resistance to cold or the protection of Canadian forests. *To achieve this goal, RNA Canada ARN aims to accelerate the development of candidate biologics from the academic sector and foster national partnerships between industry and academia.* The recent surge in RNA discoveries and the speed with which the RNA discovery pipeline can lead to tangible translational and clinical advances is generating significant interest from the private sector. This refocusing on RNA in the biotechnology industry would benefit from close interactions with RNA experts. As the need for academia-industry funding is therefore expected to multiply in the very near future, this funding initiative based on the needs of the industrial sector should facilitate the productive integration of RNA discoveries.

- c. **New technology Platforms.** Many of the above large-scale, multidisciplinary projects and their applications will require technological platforms adapted to the needs of the RNA researchers and incorporating emerging methods and tools, such as RNA/Biofoundaries and spatial genomics. Several existing platforms including RNomics, or AI may be particularly suited to provide services dedicated to RNA scientists or they may themselves be conducting projects that tailor tools or adapt technologies for general use. Given the potential for RNA research to benefit human health, **RNA Canada ARN** wishes to encourage projects that will maximize this interface by proposing innovative ways to link RNA science with, for example, clinical data, or the recruitment of dedicated patient cohorts. It will be a priority to ensure that similar links with forestry, environment and agriculture are developed.

2) to empower Canadian RNA scientists to lead **International Consortium Initiatives** (ICIs) in RNA-based approaches. Accordingly, a strategic program dedicated to establishing a network of international researchers under the leadership of one or several Canadian scientists will be established. Establishing international partnerships based on complementary expertise can create new paths to innovation, training, and application, and can provide a leverage effect for investments and enable Canada to capitalize on discoveries and leapfrogging technologies.

3) to **develop, recruit and retain essential talent** to take advantage of the new investments in RNA technologies. It is crucial for the life sciences and bio-manufacturing ecosystems in Canada to increase education and training budgets and engage in continuous reskilling of staff. There is a desperate need for continuous training on RNA technologies for staff already in place and for advanced training dedicated to these technologies for current and future students. Targeted training in the RNA sector will promote knowledge of RNA technologies, bio-manufacturing, and entrepreneurship.

4) to promote RNA science by **informing and educating** the public and all stakeholders of the potential of RNA-based technologies. As RNA becomes a mainstream conversation, this will contribute to attracting and retaining the next generation of RNA scientists. Dedicated conference series and town hall meetings will help raise awareness of the tremendous Canadian expertise by media, young adults, and policymakers. GE³LS research investigates the intersection of genomics and society and will provide insights into public values, ethics, economics, environmental impacts, legal and social policy issues related to RNA genomic science, critical for the societal buy-in to disruptive emerging technologies and innovation in the RNA sciences This concept will be expanded by considering the United Nations' 17 Sustainable Development Goals (SDGs), which are an urgent call for action by all

countries in a global partnership. SDGs recognize that strategies that improve health and education, and spur economic growth must reduce inequality, climate change and contribute to preserve our oceans and forests

RNA Canada ARN therefore plans to work **in collaboration with Tri-Council and Genome Canada** to develop these new funding programs (which will be distinct from existing programs) that will target the needs of the academic and industrial sectors while encouraging interactions between them. **RNA Canada ARN** *proposes the creation of a new dedicated peer-review program, managed by existing granting agencies (including Genome Canada) funded by federal and provincial governments, industry, and philanthropy.*

To accomplish these objectives, we have established a Science Industry Advisory Committee (SIAC) to strategically advise a team of high-level managers, mastering RNA technologies and having a strong knowledge of the ecosystem. This team will be responsible for the operationalization of the five-year strategy and the implementation of the objectives listed above. As a central access point for RNA research in Canada, this team of professionals will contribute directly to **development of partnerships** to ensure a match between industry needs and those of the research community, and to attract **international** research co-financing both for the academic and industrial sectors.

RNA CANADA will support efforts (canvassing, networking, support for project preparation, etc.) to obtain funds for collaborations and partnerships. **RNA Canada ARN** will support project teams throughout the preparation of research proposals and will also be able to advise project managers on the funding structure of such projects to maximize the sustainability of funding.

The team will also promote the establishment of structured collaborations with other national and international initiatives and networks. Among their various responsibilities, will be to create a central registry and a website of information on researchers, target areas, industry partners, platforms, and grant opportunities to facilitate planning, communication and creation of partnerships. The establishment of workshops and the organization of town hall meetings will help develop partnerships with organizations from different sectors of activity to better understand the environments, needs, and the possibilities of co-development.

To carry out the above objectives, an operating budget of \$1.2M per year is required (\$6M over the next 5 years).