

Sector: Biopharmaceutical**Sub-sector:** Infectious diseases HIV/AIDS

Nucleic acid hairpins as inhibitors of HIV RNase H

Information Summary

Reference Code:	ROI 03050
Technology overview:	First in class selective inhibitors of RNase H activity of HIV Reverse Transcriptase
Applications:	Biopharmaceutical composition indicated for the management of HIV infection.
Validation:	Preclinical enzyme and cell assays.
Inventors:	Damha, Masad et. al
Opportunity :	The RNase H domain of the RT is a strategic target for therapeutic intervention
Deal terms:	Exclusive or non-exclusive license to pending U.S. patent application and continuations.
Contact:	John DiMaio Ph.D. 514-398 8949 john.dimaio@mcgill.ca

Technology Description

This technology provides novel inhibitors of HIV-1 RT RNase H. The compounds of the invention are “first in class” and characterized as low molecular weight oligonucleotide hairpins. At concentrations tested, the compounds have no effect on human cellular RNase H and are resistant to degradation by cellular nucleases in vitro. These hairpins do not appear to block the incorporation of chain-terminators such as AZT or 3TC, and do not appear to occupy the NNRTI binding site. Thus, they have the potential to act synergistically with both NRTIs and NNRTIs. The compounds of this invention form the basis of drug discovery and optimization of novel clinical candidates targeted to HIV RNase H.

Medical and market need:

Since the beginning of the pandemic, the HIV virus has

infected more than 50 million people worldwide and is responsible for over 14 million deaths due to AIDS or AIDS-related complications. While HIV/AIDS is a global socioeconomic concern, the burden of disease in industrialized nations remains the principal driver of new product offerings. Antiretrovirals (ARV) comprising combination drug regimens remain the cornerstone therapy providing: (i) sustainable efficacy, (ii) patient compliance and (iii) cost effectiveness. Although the virally encoded RT is an attractive drug target, it is an error prone enzyme, which contributes to the enormous genetic variability of the virus, and, in turn, to the development of mutations responsible for emergence of resistance to drug regimens in clinical practise.

Opportunity:

Current antiretroviral therapy comprises combination drug regimens (coined HAART- *highly active antiretroviral therapy*) generally consisting of two NRTIs and a protease inhibitor and/or a non-nucleoside reverse transcriptase inhibitor (NNRTI). This combination has been shown to suppress viral load significantly and for prolonged periods. The emergence of resistant HIV strains demands alternative strategies as provided, for example, by virus entry or fusion inhibitors, *e.g.* FUZEON™. Rapid (pre)clinical development and fast-track designation of candidate drugs for HIV infection continues to create opportunity for innovative product offerings. HIV RT is a multifunctional enzyme that possesses properties of a DNA polymerase on both RNA and DNA templates as well as ribonuclease H (RNase H) activity. Both the RT-associated DNA polymerase and RNase H activities are required to convert the single-stranded RNA genome into double-stranded DNA that is then integrated into the host chromosome.

The RNase H domain of the RT is a strategic target for therapeutic intervention because RNase H activity of HIV-1 RT is vital for viral replication.

Office of Technology Transfer

McGill University
1555 Peel Street, 11th floor
Montreal, Quebec, Canada H3A 3L8

Bureau de Transfert de Technologies

Université McGill
1555 rue Peel, 11ième étage
Montréal, Québec, Canada H3A 3L8

Tel.: (514) 398-4200
Fax: (514) 398-1482
www.techtransfer.mcgill.ca



Masad J. Damha Ph.D.

Professor; Department of Chemistry, McGill University

B.Sc. 1983, Chemistry McGill University

Ph.D. 1988 Chemistry McGill University under the direction of Prof. Ogilvie.

Assistant Professor; University of Toronto's Erindale College. 1992, he returned McGill University, as James McGill Professor of Chemistry.

Director of Graduate Studies in the Department of Chemistry.

Co-Founder of Anagenis Inc.

Scientific Advisory Board of Topigen Pharmaceuticals.

Board Member of the Oligonucleotide Therapeutic Society (2008-) and International Society of Nucleosides Nucleotides and Nucleic Acids (2006-); Editorial Board of the journal *Bioconjugate Chemistry* (1999-2003), and the Accreditation Committee (1999-2001) & Award Selection Committees of the Canadian Society for Chemistry.

Research focus: Chemistry & Biology of Nucleic Acids

Professor Damha has 25 years experience in nucleic acid chemistry and has authored more than 130 publications and patents worldwide. Prof. Damha's research group has made important contributions to nucleic acid chemistry at the interface between chemistry and molecular biology. His research group has been studying DNA mimics as model systems for down-regulating gene expression. The arabinose-based compounds developed by his research group will enter clinical trials in 2009 for the management of chronic obstructive pulmonary disease. Among his major awards are the John Charles Polanyi Chemistry Prize (Ministry of Colleges and Universities, 1989), The IUPAC Award (Chemical Institute of Canada, 1991), Ichikizaki Award for Young Chemist (1989-94), the Merck-Frosst Award for Therapeutic Research (Canadian Society for Chemistry, 1999), Fellowship of the Chemical Institute of Canada (F.C.I.C., since 1999) and the Bernard Belleau Award (Canadian Society for Chemistry, 2007)

Masad J. Damha, Ph.D.

Professeur au Département de Chimie, Université McGill

B.Sc. Chimie, Université McGill (1983)

Ph.D. Chimie, Université McGill (1988) sous la supervision du Professeur Ogilvie.

Professeur adjoint à la Chaire; University of Toronto's Erindale College. En 1992, il se joint de nouveau à l'Université McGill, à titre de professeur James McGill en chimie.

Directeur des cycles supérieurs du Département de chimie

Cofondateur de Anagenis Inc.

Membre du Conseil scientifique consultatif de Topigen Pharmaceuticals

Membre du Comité de rédaction du journal *Bioconjugate Chemistry* (1999-2003), du Comité d'agrément (1999-2001) et du Comité de sélection des prix de la Société canadienne de chimie

But de la recherche : Chimie et biologie des acides nucléiques

Le professeur Damha compte 25 ans d'expérience en chimie des acides nucléiques et il est l'auteur de plus de 130 publications et brevets à l'échelle internationale. Son groupe de recherche a fait des contributions importantes à la chimie des acides nucléiques, à l'interface de la chimie et de la biologie moléculaire. Il étudie les analogues de l'ADN comme systèmes modèles de dérégulation de l'expression génique. Les composés synthétisés à partir de l'arabinose mis au point par le groupe de recherche du professeur Damha sont actuellement au stade du développement clinique pour la prise en charge de la maladie pulmonaire obstructive chronique. Le professeur Damha a reçu des prix prestigieux, notamment le Prix de chimie John Charles Polanyi (ministère de la Formation et des Collèges et Universités, 1989), le Prix IUPAC (Institut de chimie du Canada, 1991), le Prix Ichikizaki pour les jeunes chimistes (1989-1994), le Prix Merck-Frosst de la recherche thérapeutique (Société canadienne de chimie, 1999), le titre de boursier de l'Institut de chimie du Canada (depuis 1999) et le Prix Bernard-Belleau (Société canadienne de chimie, 2007).