



CORPORATE PRESENTATION -NON-ADDICTIVE ENDOGENOUS, OPIOID- BASED ANALGESICS

JANUARY 2024

CSE: PREV
OTCQB: PRVCF
FSE: 18H



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CORPORATE OVERVIEW

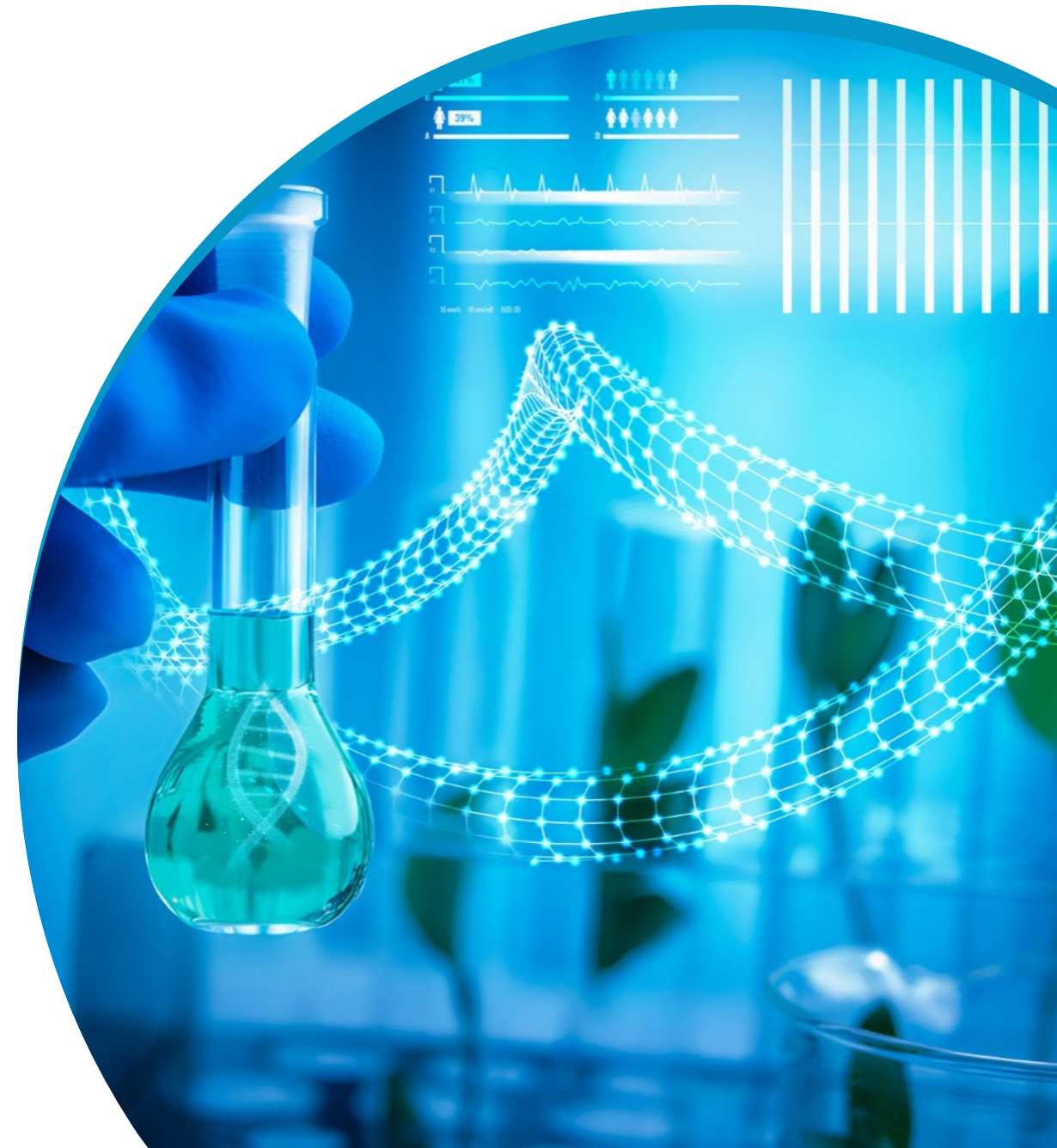
Preventive health sciences company with corporate offices in Vancouver, Canada, and wholly owned subsidiary in Brisbane, Australia.

Leveraging innovative science & technology to enhance natural products as novel targeted therapeutics in a diverse portfolio of R&D programs addressing significant life-affecting diseases.

Focus on developing Nature Identical® products and therapies for health-conscious consumers and becoming a trusted provider of preventive health solutions globally.

Building an extensive library of intellectual properties to enter into JV, development and licensing agreements with leaders in pharmaceutical and cannabis industries.

Artificial Intelligence & Machine Learning is being implemented to enhance, accelerate and predict outcomes, processes and solutions, amongst other selected data. Our domain www.preveceutical.ai will be developed.



CORPORATE OVERVIEW

OPIOID CRISIS – THE FACTS

Since 1999, >600,000 people in the USA & Canada have died from an opioid overdose¹ In addition, millions more became addicted or were seriously/irreversibly harmed Mortality rates in each country exceeds that of the worst of the HIV/AIDS epidemic.

OPIOID CRISIS – THE FIGURES

In the USA & Canada, 2020 was the worst year on record for fatalities both in terms of number of deaths and % increase year-on-year:

- › Opioid toxicity deaths in Canada increased **63%** to 6,214, from 3,830 the prior year;
- › Opioid overdoses in the USA rose **37%** from 50,963 to 69,710, bringing the total of such deaths since 1999 to over 583,000.

Safely & effectively treating moderate-to-severe pain with engineered, metabolically stable endogenous opioid peptides – harnessing the body's own painkillers

Our proprietary library of stabilized (linear & cyclic) peptides selectively target the endogenous kappa-opioid receptor pathway, blocking pain at its source in the peripheral nervous system...

¹Centers for Disease Control and Prevention. Multiple Cause of Death. In: Statistics NCH, editor. 2021.

²Luo F, Li M, Florence C. State-Level Economic Costs of Opioid Use Disorder and Fatal Opioid Overdose - United States, 2017. MMRW Morb Mortal Wkly Rep 2021; 70(15): 541-6.

³Centers for Disease Control and Prevention. HIV surveillance—United States, 1981–2008. MMRW Morb Mortal Wkly Rep 2011; 60(21): 689–93.

⁴Jonah L, Bourgeois AC, Edmunds M, Awan A, Varsaneux O, Siu W. AIDS in Canada—Surveillance Report, 2016. Can Commun Dis Rep 2017; 43(12): 257–61.

⁵Lancet. 2022 Feb 5;399(10324):555-604.

⁶<https://patentscope.wipo.int/search/en/detail.jsf?docId=CA391585396>

⁷<https://patentscope.wipo.int/search/en/detail.jsf?docId=EP412600121>

NON-ADDICTIVE ANALGESIC PEPTIDES FOR PAIN MANAGEMENT

SELECTIVELY TARGETING THE KAPPA-OPIOID RECEPTOR

A panel of peptides was designed and evaluated in a rodent model of inflammatory pain, demonstrating exquisite potency, with analgesia matching and even exceeding that of clinically used opiates.

Through systematic evaluation, a library of proprietary peptides (linear & cyclic) that selectively target KOR, have extended activity (hours), and are devoid of tolerance while demonstrating predictable degradation profiles enabling safe and reproducible re-dosing have been developed.

We have meticulously screened the fragments derived from D1-17, identifying those that are primarily responsible for potent analgesia, as well as identifying cleavage sites which lead to rapidly diminished analgesia.

01.

06.

02.

05.

03.

04.

Clinically available opioid analgesics primarily target the Mu-opioid (MOR) receptor while also hitting targets in the central nervous system (CNS), leading to serious/debilitating side effects including addiction, tolerance, respiratory depression and constipation, with overdose-related deaths plaguing society globally.

Our strategy limits targeting to the tissue of the peripheral nervous system only while being highly selective in targeting the Kappa-opioid receptor (KOR) only, with the goal of exploiting the body's own (i.e. endogenous) highly potent dynorphin-17 (D1-17), antinociceptive peptide.

Immune cells release D1-17 peptide at the site of tissue injury, producing immediate, highly potent, but short-lived (secs-min) analgesia. D1-17 rapidly degrades into smaller fragments. These fragments hold the key to engineering KOR-selective, highly potent and longer-lived analgesics that can serve as next-generation pain medications.

NON-ADDICTIVE ANALGESIC PEPTIDES FOR PAIN MANAGEMENT

SELECTIVELY TARGETING THE KAPPA-OPIOID RECEPTOR

The following four stages spanning drug discovery-thru-preclinical proof-of-concept studies have been successfully completed:

STAGE 01



In silico design of Dynorphin (DYN)-based peptide fragments and opioid receptor docking/affinity screening studies.

STAGE 02



Iterative design and synthesis of DYN fragment peptide libraries with in vitro screening of kappa-opioid receptor selectivity and metabolic stability.

STAGE 03



Engineering of metabolically-stabilized DYN peptide libraries (linear and cyclized), retaining exquisite KOR-selectivity while displaying reduced desensitization and biased-signaling.

STAGE 04



Select peptides evaluated in Freud's Complete Adjuvant (FCA) rodent model of inflammatory pain, demonstrating analgesia comparable to the clinically used opiates.

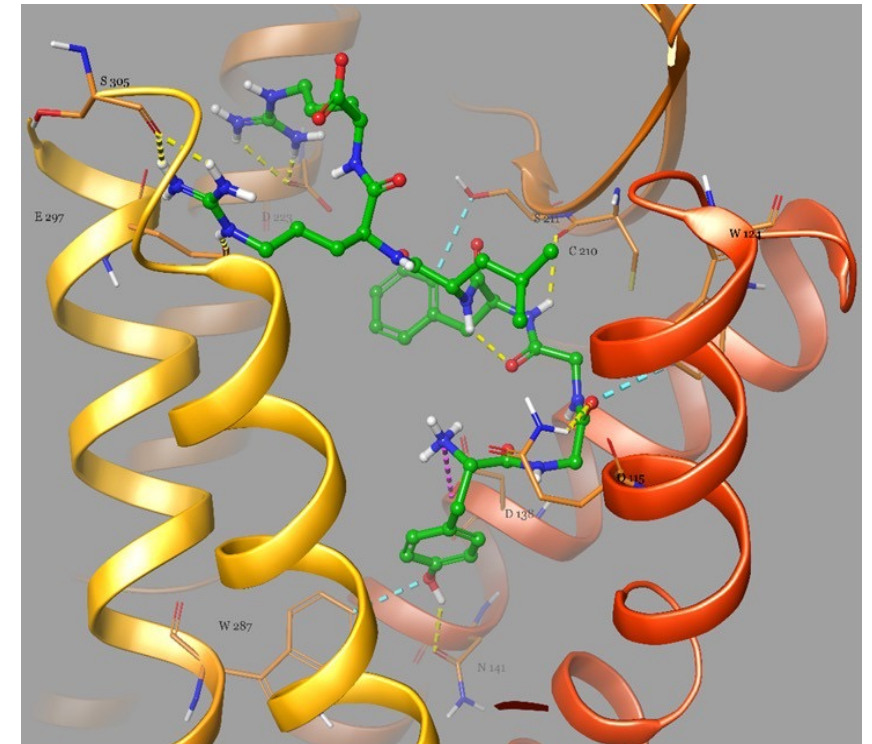
NON-ADDICTIVE ANALGESIC PEPTIDES FOR PAIN MANAGEMENT

SELECTIVELY TARGETING THE KAPPA-OPIOID RECEPTOR

STAGE 1 COMPLETED

STAGE 1: In silico design of Dynorphin (DYN)-based peptide fragments, and opioid receptor docking/affinity screening studies.

- › Using DYN1-7 as our model fragment, a library of >100 linear peptides residues in the pharmacophoric region (c.f DYN1-7, see left image) and non-natural amino acids rationally positioned were initially screened and analyzed in silico.
- › The impact/role of each amino acid in the dynorphin peptide sequence on KOR-affinity and stability was derived, with only one modification/amino acid substitution undertaken at a time between iterations of sequence design and analysis.
- › The top 50 virtual peptide 'hits' from systematic and meticulous in silico studies were progressed to Stage 2.



Dynorphin 1-7 (DYN1-7) interactions bound to the human KOR active site.

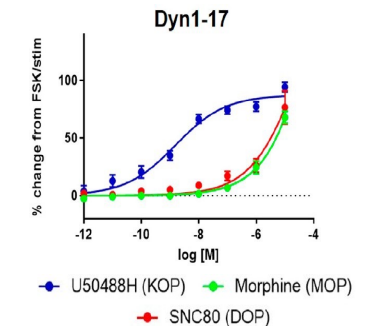
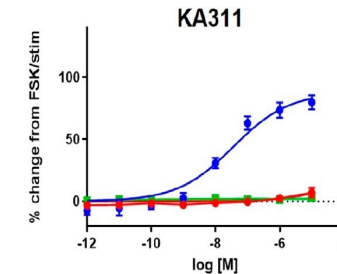
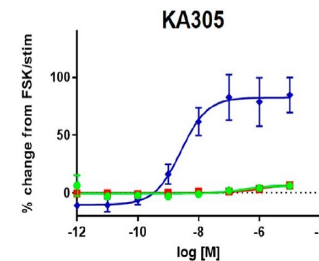
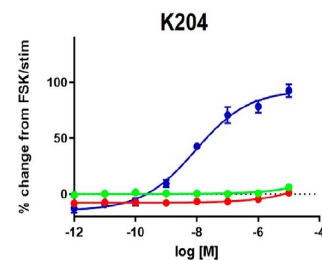
NON-ADDICTIVE ANALGESIC PEPTIDES FOR PAIN MANAGEMENT

SELECTIVELY TARGETING THE KAPPA-OPIOID RECEPTOR

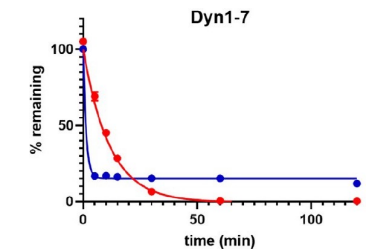
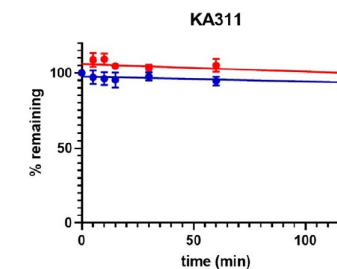
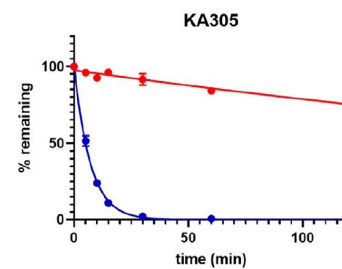
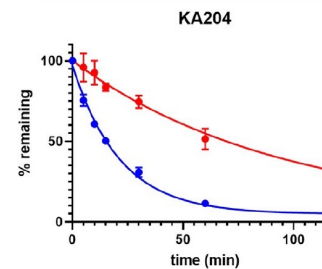
STAGE 2 COMPLETED

STAGE 2: Iterative design and synthesis of DYN fragment peptide libraries with in vitro screening of kappa-opioid receptor selectivity, and metabolic stability.

- › Top Panel: In vitro screening of select peptides derived from Stage 1, confirms highly selective KOR activity in the cyclic AMP (cAMP) assay, using KOP (U50488H), MOP (morphine) and DOP (SNC80) selective agents for comparison.
- › Bottom Panel: Confirms enhanced stability & predictable degradation of select peptides (c.f. DYN1-7) in biological milieu (red – rat plasma; blue – trypsin) encountered in vivo.



Concentration-response curves of select peptides in the cAMP assay, compared to reference peptide Dyn1-17. HEK293-KOR cells – blue, HEK293-MOP cells – green, HEK293-DOP cells – red.

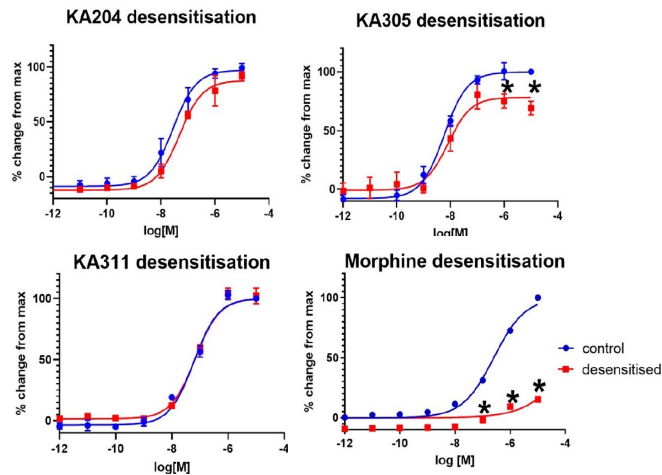


NON-ADDICTIVE ANALGESIC PEPTIDES FOR PAIN MANAGEMENT

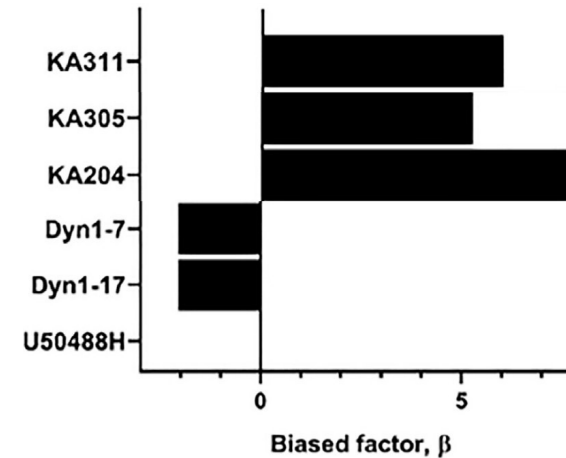
SELECTIVELY TARGETING THE KAPPA-OPIOID RECEPTOR

STAGE 3 COMPLETED

STAGE 3: Engineering of metabolically-stabilized DYN peptide libraries (linear and cyclised), retaining exquisite KOR-selectivity while displaying reduced desensitization, and biased-signaling.



Left Panels: KOP receptor desensitization in cAMP assay in response to select peptides, compared to MOP desensitization in response to morphine (MOP cells), the latter of which results in comprehensive desensitization—blue – first dose; Red – second dose.



Right Panel: Determination of bias factor β , relative to U50488H, for control compounds and select peptides. Positive values indicate a bias towards cAMP modulation (desired), which the selected peptides all display, whereas negative values indicate a bias towards pERK (undesired).

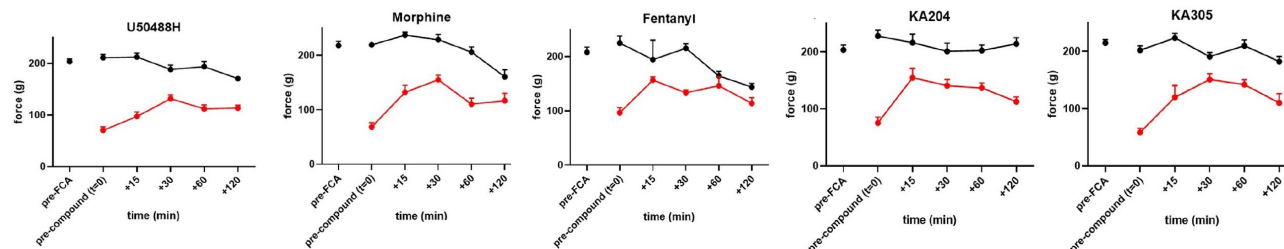
NON-ADDICTIVE ANALGESIC PEPTIDES FOR PAIN MANAGEMENT

SELECTIVELY TARGETING THE KAPPA-OPIOID RECEPTOR

STAGE 3 COMPLETED

STAGE 4: Select peptides evaluated in a Freund's Complete Adjuvant (FCA) rodent model of inflammatory pain, demonstrating analgesia comparable to the clinically used opiates.

- › In vivo testing in the Freund's Complete Adjuvant (FCA) model of inflammatory pain was pursued with a panel of select peptides, which were compared with U50488H, morphine, and fentanyl.
- › Administration of U50488H (KOP receptor agonist; positive control) to the inflamed paw caused an increase in paw withdrawal threshold (in grams) characteristic of an opioid-like antinociceptive effect.







Plots of threshold of paw withdrawal to mechanical stimulus, over time as measured by Randall-Selitto assay, in the FCA model of inflammatory pain. Force (g) required to elicit a paw-withdrawal response for individual compounds tested in the FCA-treated paw (red) and un-inflamed paw (contralateral, black), after compound administration (i.e. after t=0).

- › All three reference compounds, U50488H, morphine and fentanyl displayed effects in the contralateral (uninflamed and untreated; black line) control paw by 120 min following its administration into the ipsilateral paw.
- › These acute allodynia-inducing (i.e. painful, when pain should be absent) effects were not displayed by our select peptides.

NON-ADDICTIVE ANALGESIC PEPTIDES FOR PAIN MANAGEMENT

SELECTIVELY TARGETING THE KAPPA-OPIOID RECEPTOR

COMPLETED STUDIES

- › **STAGE 1:** In silico design of Dynorphin (DYN)-based peptide fragments and opioid receptor docking/affinity screening studies. 
- › **STAGE 2:** Iterative design and synthesis of DYN fragment peptide libraries with in vitro screening of kappa-opioid receptor selectivity and metabolic stability. 
- › **STAGE 3:** Engineering of metabolically-stabilized DYN peptide libraries (linear and cyclized), retaining exquisite KOR-selectivity while displaying reduced desensitization and biased-signaling. 
- › **STAGE 4:** Select peptides evaluated in Freud's Complete Adjuvant (FCA) rodent model of inflammatory pain, demonstrating analgesia comparable to the clinically used opiates. 

PROPOSED STUDIES WITH LINEAR & CYCLISED PEPTIDES

- › Tolerance and addiction studies in appropriate preclinical pain models
- › Expanding evaluation of peptides to a broader range of pain types, e.g. neuropathic pain, chemotherapy-induced pain, etc.
- › Dose escalation and toxicity study in large animal pain model, e.g. NHP.
- › First, in the human non-inferiority trial, comparing efficacy & side effects to opiates, e.g. morphine.

NON-ADDICTIVE ANALGESIC PROJECT

PATENT FAMILY

PATENT NAME	COUNTRY	FILING DATE	PUBLICATION DATE
DISULFIDE BOND CONTAINING COMPOUNDS AND USES THEREOF	INTERNATIONAL AUSTRALIA EUROPE CANADA USA	26.07.2018 15.12.2022 26.07.2018 26.07.2018 11.05.2023	31.01.2019 02.02.2023 03.06.2020 31.01.2019 11.05.2023
PEPTIDES AND USES THEREOF	INTERNATIONAL EUROPE CANADA AUSTRALIA	01.07.2021 01.07.2021 01.07.2021 01.07.2021	06.01.2022 10.05.2023 06.01.2022 06.01.2022
CYCLIC PEPTIDES AND USES THEREOF	INTERNATIONAL AUSTRALIA CANADA EUROPE USA	24.01.2020 24.01.2020 24.01.2020 24.01.2020 24.01.2020	30.07.2020 30.07.2020 30.07.2020 30.07.2020 30.07.2020

PREVECEUTICAL TEAM



Stephen Van Deventer
– Chairman and Chief Executive Officer

Mr. Van Deventer is an experienced businessman and corporate director. Specializing in international corporate relations and business development over the last thirty-five years, Mr. Van Deventer has focused on launching small to medium-sized companies into the public markets in Canada, the United States, Europe and Australia. He has also owned and operated private companies.



Mak Jawadekar PhD
– President, Chief Science Officer and Director

Dr. Jawadekar completed his Ph.D. in Pharmaceutics at the University of Minnesota. Dr. Jawadekar worked at Pfizer Inc. for twenty-eight years, where he most recently acted as the Director of Portfolio Management. During his career, he was responsible for drug delivery technology assessments involving external drug delivery technologies. Dr. Jawadekar has extensive experience in creating and cultivating external partnerships and alliances for drug delivery technologies.

PREVECEUTICAL TEAM



Linnéa Olofsson PhD
– Director

Dr. Olofsson is an accomplished biophysicist with 12 years of laboratory research experience in academia, and 3 years working in the private sector as scientific support and equipment sales. She successfully advances science by providing counsel and training to the scientific community, contributing to executing strategic marketing plans by working in conjunction with the sales team members to identify and qualify sales leads through technical discussions. Dr. Olofsson closely collaborates with corporate strategic decision-making processes to penetrate new market applications to increase return on investment.



Kathy Rokita CPA
– Director

Ms. Rokita is a finance, operations, and strategy-focused executive having extensive experience with large medical groups. Her involvement includes business development, information reporting, analytics, and improvements in financial performance and operational processes. She has a background in treasury management, budgeting, as well as mergers and acquisitions. Kathy has been appointed to PreveCeutical's audit committee. Kathy also selflessly dedicates time to volunteering as a board member for St. Vincent Hospital Foundation and Angelman Syndrome Foundation, where she served as Treasurer and President of the Board of Directors.

PREVECEUTICAL TEAM



C. Evan Ballantyne
– Director

Mr. Ballantyne has extensive executive leadership experience and has spent the last 20 years as a public and private company Chief Financial Officer in the healthcare industry. He was most recently the CFO of OncXerna Therapeutics Inc. where he worked to advance partnering opportunities for the company's biomarker program. Prior to OncXerna, Ballantyne was CFO at Orchestra BioMed Inc. where he assisted with the closing of two equity financing rounds with proceeds of \$57 million. At Orchestra, he also helped close a global partnership deal valued at more than \$200 million.



Harry Parekh PhD, BSc Hons I
– Chief Research Officer

Based at the University of Queensland's (UQ) Pharmacy Australia Centre of Excellence (PACE) in Australia, Dr. Parekh also holds an adjunct faculty position at Manipal University, India. Dr. Parekh heads the Drug/Gene Delivery Group at PACE-UQ with his team developing highly innovative and translational medicine delivery systems in-conjunction with physicians whose expertise span cancer, obesity-&-diabetes, macular disease, infectious disease, and neurological conditions.

PREVECEUTICAL TEAM



Shawn Sadler
– Head of Artificial Intelligence

With a deep understanding of Data Management, AI Frameworks, Information Governance, and Machine Learning, Mr. Sadler will bring valuable insights and strategic thinking to PreveCeutical. His expertise in network design and engineering, combined with his exceptional project management skills, make him an invaluable asset. Shawn will align PreveCeutical business objectives to bring ground-breaking products to market with emerging AI solutions to maximize performance.



Andrea Ortega
– Executive Assistant & Office Manager

Ms. Ortega is a professional currently studying commerce while gaining valuable experience in the hospitality and marketing industries over the past two years.

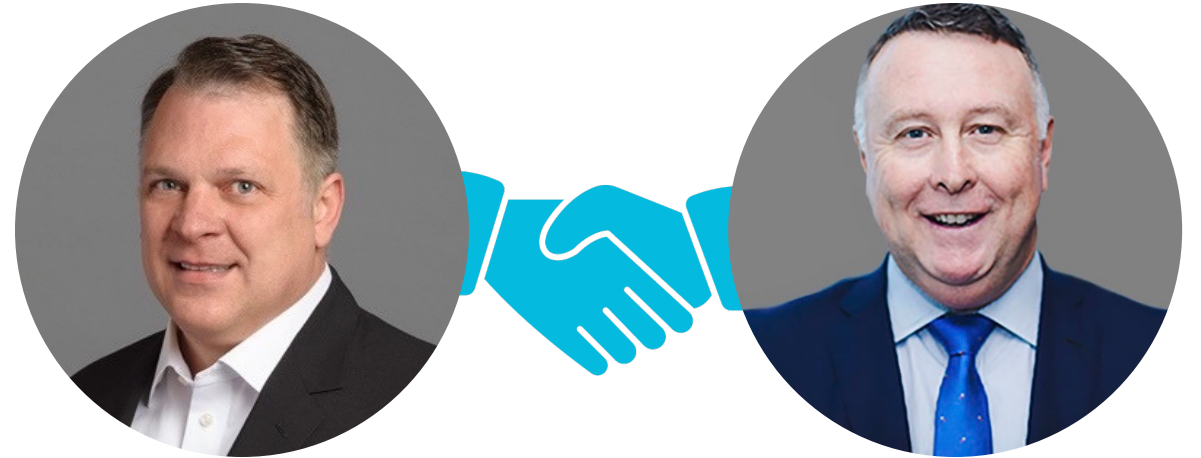
Ms. Ortega excels at streamlining operations and optimizing marketing strategies, all while serving as an accomplished executive assistant.

PREVECEUTICAL AUSTRALIA TEAM

PreveCeutical® has established a wholly-owned subsidiary in Brisbane, Queensland, Australia, to bolster their research and development interests.

The Australian team, which will be led by Stephen Van Deventer, the Chief Executive Officer, will work closely with Dr. Harry Parekh, PreveCeutical's Chief Research Officer, to advance the company's therapeutic pipeline.

The office will also allow for better engagement with commercial partners on other ventures that PreveCeutical is pursuing in the region.



Stephen Van Deventer
Chairman and Director

James Henderson
Independent Director

RESEARCH COLLABORATORS



Murdoch
UNIVERSITY

Dr. Rakesh Veedu is leading the Precision Nucleic Acids Theranostics Group, as a McCusker Research Fellow with the Perron Institute for Neurological and Translational Science, based at the Centre for Comparative Genomics at Murdoch University (Perth, Australia). He is an emerging expert internationally in the field of molecular medicine, using nucleic acid-based biotechnologies and developing novel nucleic acid as potential drug therapies for a range of neurological diseases, genetic disorders and solid cancers.



QIMR Berghofer
Medical Research Institute

Professor Grant Ramm is currently the head of the Hepatic Fibrosis Laboratory and Coordinator of the Cell and Molecular Biology Department at QIMR-Berghofer, a leading medical research institute located in Brisbane, Australia.

RESEARCH COLLABORATORS

Dr. Ajit Shetty

Dr. Shetty has extensive pharmaceutical experience leading commercial and supply chain operations as well as significant educational background including a PhD in Metallurgy from Trinity College at Cambridge University. Dr. Shetty spent 36 years at Johnson & Johnson (“J&J”) in a wide range of global roles. From 2007 to 2012, he served as Corporate Vice President, Enterprise Supply Chain reporting to the CEO and was responsible for the transformation and optimization of J&J’s supply chain. In addition, from 2004 to 2012, he served as chairman of Janssen Pharmaceutical.

Aditya Bahl

Mr. Bahl brings over 20 years of experience in pharmaceutical marketing and clinical development and is known for his entrepreneurship and creativity. He is the CEO and founder of RAS LSS, a boutique healthcare consulting group based in Germany providing strategic guidance to biotechnology and pharmaceutical companies on franchise and product strategy, clinical development and commercialization.

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