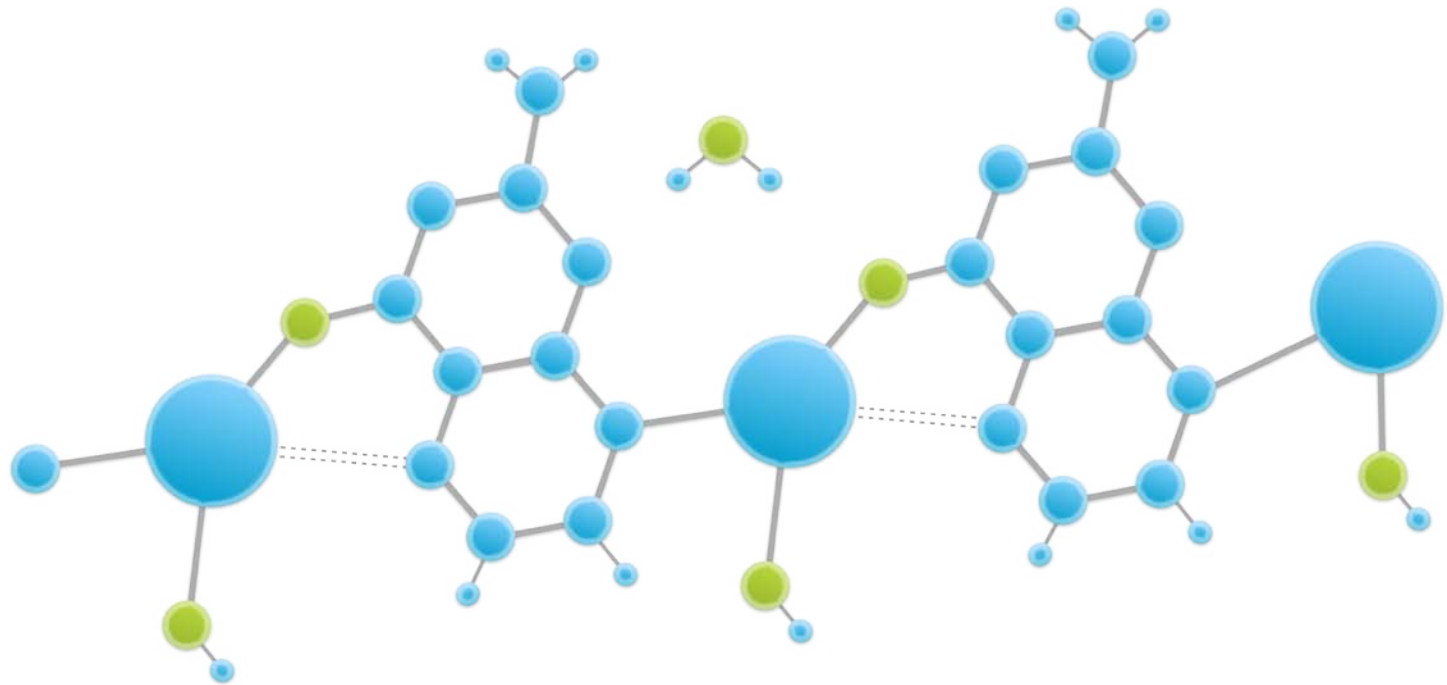


Calcium Pterin Oral Immunotherapies



The Calcium Pterin Story

- Pterins (from the Greek pteron = wing) are naturally-occurring heterocyclic compounds responsible for the vibrant color of butterfly wings
- 1970's @UCLA: A fluorescent blue spot was consistently observed in the chromatograms of urine from cancer patients
- The blue spot is determined to be pterin-6-aldehyde
- Several pterins were subsequently shown by high pressure liquid chromatography to have altered concentrations in the urine of cancer patients



The Calcium Pterin Story

- Search of scientific literature revealed some pterins possess anti-tumor and immuno-modulatory properties
- Study of the chemistry of “active” pterins led to successful testing of calcium pterin (Pterin+Calcium™) for antitumor activity
- Further refinement of the calcium pterin structure led to the synthesis DCP™ by Dr. Wolfgang Pfeleiderer, and to the *in vivo* testing and patenting of DCP by SanRx



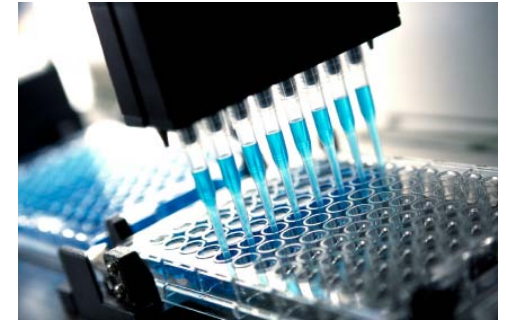


The Calcium Pterins

- Are being developed as low toxicity, orally active adjunct therapies for breast cancer and infectious diseases, operating as immunomodulators, and with other potential applications.
- Have demonstrated significant inhibition of tumor growth, chronic hepatitis B replication, and diet-induced diabetes, in mouse models, and inhibition of tuberculosis mycobacteria *in vitro*.
- Exhibit low toxicity as they are comprised of calcium and pterin, both of which are part of human chemistry.

The Calcium Pterins

- Show promising published results *in vitro* and *in vivo*
- Are covered by global patents (filed 2007-08)
- Have brought together an internationally renowned scientific advisory team
- Have prompted fundraising efforts to market Pterin+Calcium as a dietary supplement and DCP as a pharmaceutical





How SanRx Products might help

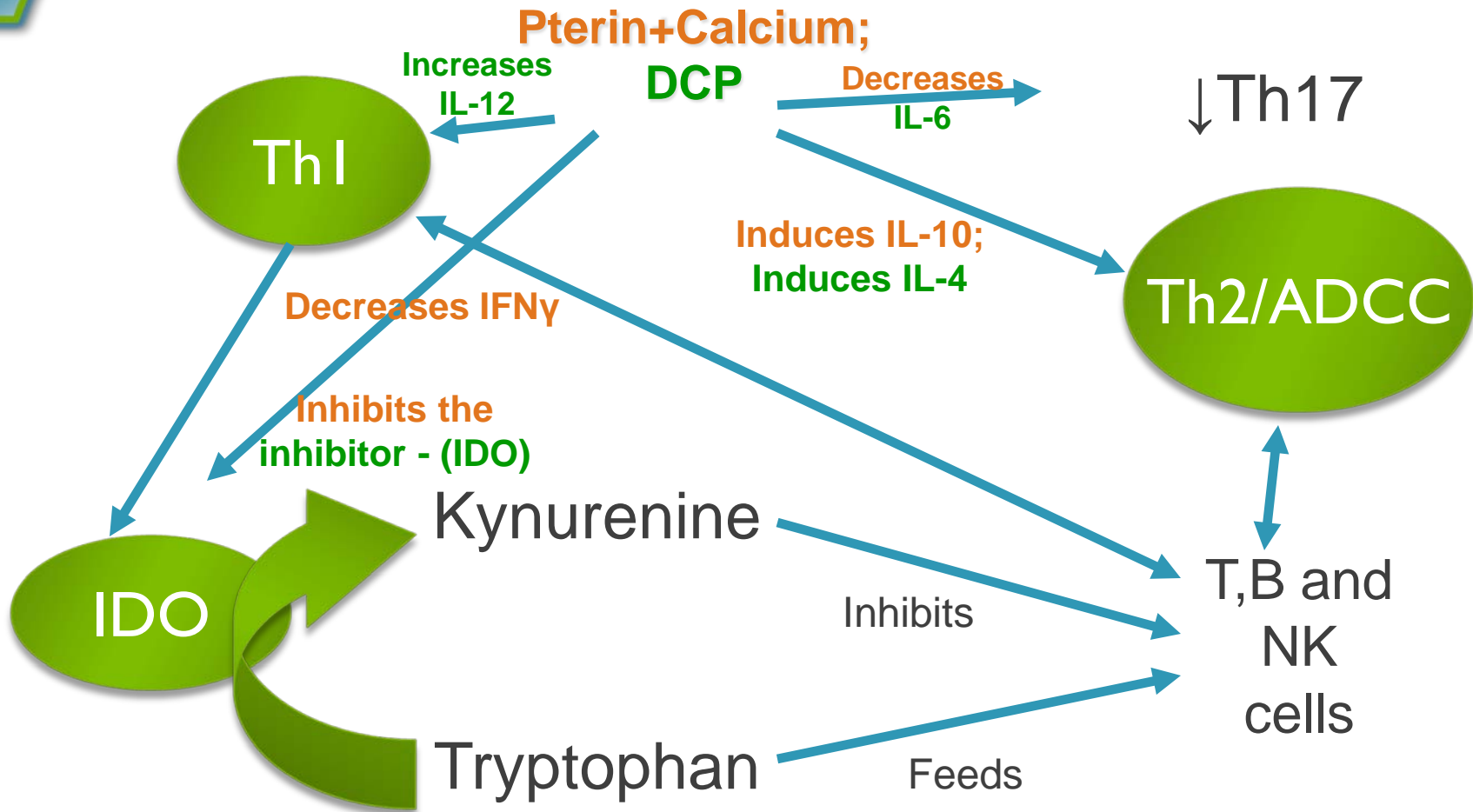
- Normally, the immune system recognizes cancer cells
- Cancer cells escape the immune system through IDO pathway
- Inhibiting IDO means that the cancer cells cannot escape the immune system

Benefits of Calcium Pterin Treatment

- New, orally available immune modulator
- No hair-loss or nausea
- New mechanism of action
- Many development opportunities / shots-on-goal



Proposed Mechanism: IDO is a Feedback Inhibitor of Th1 Inflammatory Immune Response



Reference: Terness, P., Bauer, T.M., Rose, L., Duffer, C., Watzlik, A., Simon, H., Opelz, G., 2002. Inhibition of allogeneic T cell proliferation by indoleamine 2,3-dioxygenase-expressing dendritic cells: mediation of suppression by tryptophan metabolites. J Exp Med 196, 447-457.



Calcium Pterins' Inhibition of IDO May Allow SanRx to Treat These Conditions

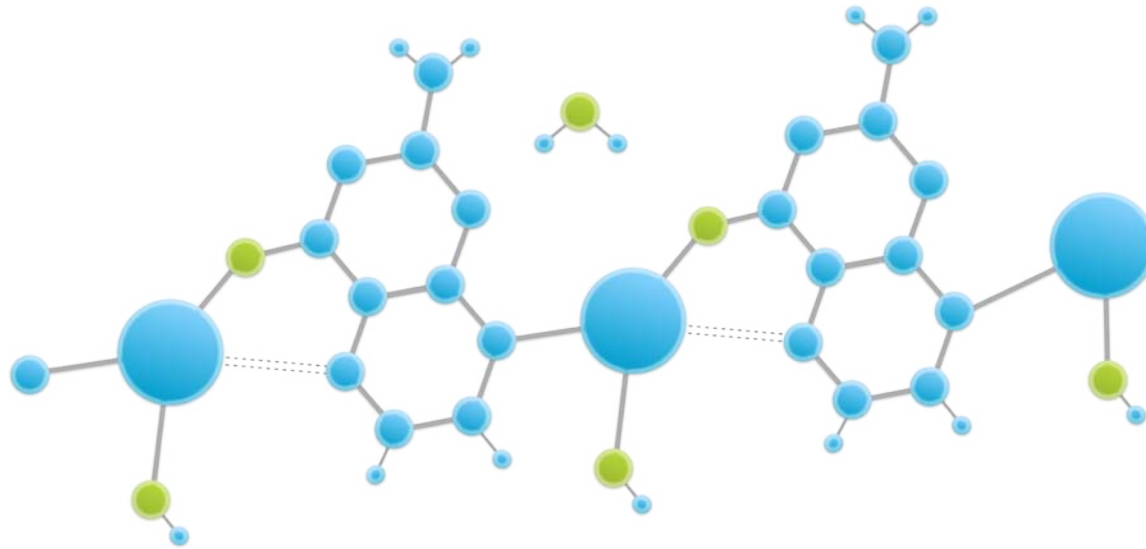
- **Cancer**
- **Infectious diseases (e.g., viral)**
 - Moheno P, Morrey J, Fuchs D. Effect of dipterinyl calcium pentahydrate on hepatitis B virus replication in transgenic mice. *J Transl Med.* 2010 Mar 31;8:32.
 - Popov A, Schultze JL. IDO-expressing regulatory dendritic cells in cancer and chronic infection. *J Mol Med.* 2008;86(2):145-60.
- **Neurodegenerative disorders (e.g., major depression, multiple sclerosis, Alzheimer's)**
 - King NJ, Thomas SR. Molecules in focus: indoleamine 2,3-dioxygenase. *Int J Biochem Cell Biol.* 2007;39(12):2167-72.
- **Arthritis**
 - Muller AJ, Mandik-Nayak L, Prendergast GC. Beyond immunosuppression: reconsidering indoleamine 2,3-dioxygenase as a pathogenic element of chronic inflammation. *Immunotherapy.* 2010 May;2(3):293-7
- **Diabetes and Tuberculosis**
 - Unpublished results



SanRx is Focused on Cancers for First Pterin+Calcium Indications

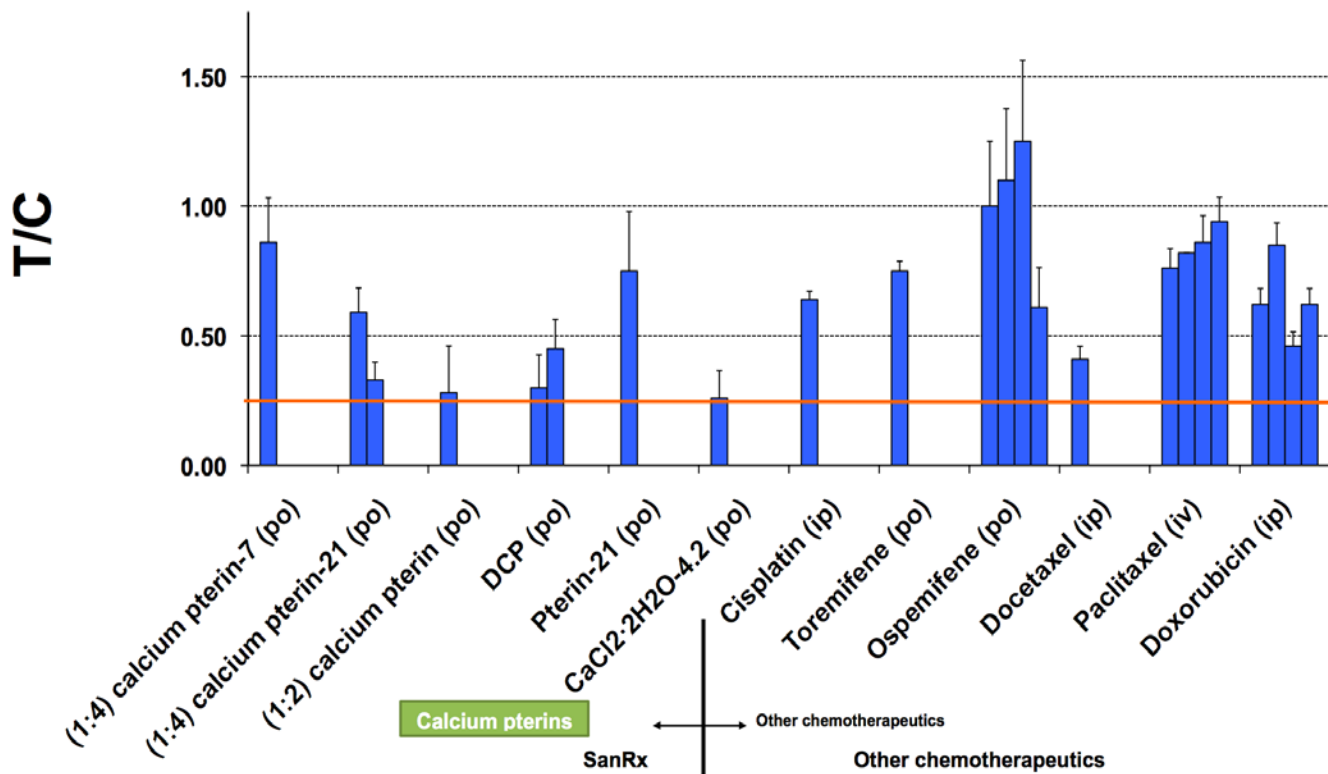
- Cancers where IDO modulation may play a role
 - **Breast Cancer**
 - Hou DY, Muller AJ, Sharma MD, DuHadaway J, Banerjee T, Johnson M, Mellor AL, Prendergast GC, Munn DH. Inhibition of indoleamine 2,3-dioxygenase in dendritic cells by stereoisomers of 1-methyl-tryptophan correlates with antitumor responses. *Cancer Res.* 2007;67(2):792-801.
 - **Squamous Cell Carcinoma**
 - Sakurai K, Enomoto K, Amano S, Kimura T, Sugito K, Kimizuka K, Ikeda T, Shibata M, Negishi N. [Study of indoleamine 2,3-dioxygenase expression in patients of esophageal squamous cell carcinoma] *Gan To Kagaku Ryoho.* 2004;31(11):1780-2.
 - **Lung Cancer**
 - Karanikas V, Zamanakou M, Kerenidi T, Dahabreh J, Hevas A, Nakou M, Gourgoulialis KI, Germenis AE. Indoleamine 2,3-dioxygenase (IDO) expression in lung cancer. *Cancer Biol Ther.* 2007;6(8):1258-62.
 - **Carcinoma of Endometrium and Uterine Cervix**
 - Sedlmayr P, Semlitsch M, Gebru G, Karpf E, Reich O, Tang T, Wintersteiger R, Takikawa O, Dohr G. Expression of indoleamine 2,3-dioxygenase in carcinoma of human endometrium and uterine cervix. *Adv Exp Med Biol.* 2003;527:91-5.
 - **Colorectal**
 - Mazzolini G, Murillo O, Atorrasagasti C, Dubrot J, Tirapu I, Rizzo M, Arina A, Alfaro C, Azpilicueta A, Berasain C, Perez-Gracia JL, Gonzalez A, Melero I. Immunotherapy and immunoescape in colorectal cancer. *World J Gastroenterol.* 2007;13(44):5822-31.
 - **Melanoma**
 - Gajewski TF. Failure at the effector phase: immune barriers at the level of the melanoma tumor microenvironment. *Clin Cancer Res.* 2007;13(18 Pt 1):5256-61.





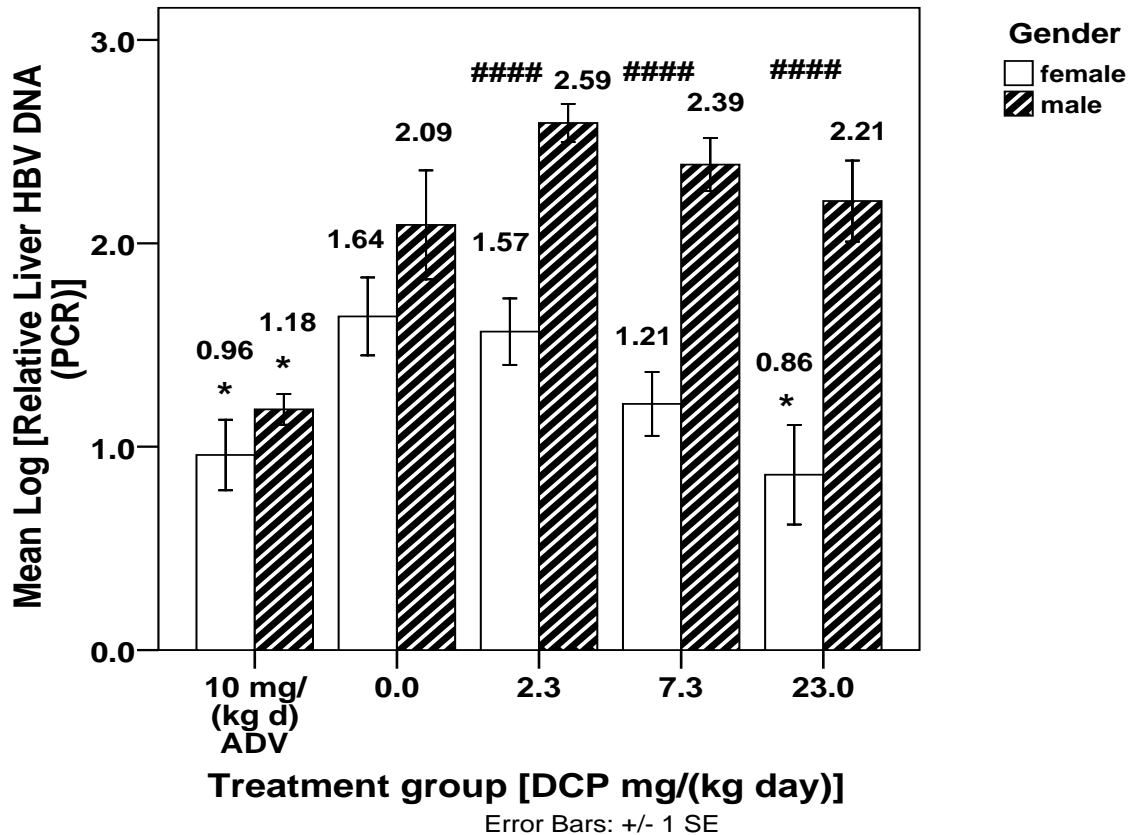
Pre-Clinical Efficacy Studies for Calcium Pterins

Calcium Pterins Compared to Common Chemotherapeutics from Published Studies: Treatment/Control (T/C) values in Nude Mice w/MDA-MB-231 After 36 days of Treatment – Lower T/C means less tumor growth



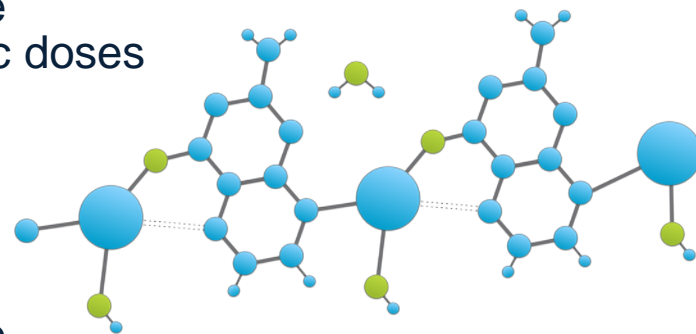
DCP Significantly Reduces Liver Hepatitis B Viral DNA in Female HBV Transgenic Mice: Comparable to Adefovir Dipivoxil (ADV)

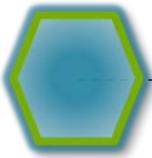
* ($p < .05$) - versus control; ##### ($p \leq .001$) – by gender



Development of DCP Followed Earlier SanRx Studies with Calcium Pterin

- Original Calcium Pterin
 - strongly inhibits spontaneous mouse mammary gland adenocarcinomas
 - inhibits human breast cancer in nude mice
 - shows no toxicity in mice at 4X therapeutic doses
 - increases plasma IL-10 in nude mice
 - decreases IL-6 & IFN- γ in nude mice
- DCP
 - inhibits human breast cancer in nude mice
 - shows no toxicity in mice at 3X therapeutic doses
 - increases plasma IL-12 & IL-4 in nude mice
 - decreases IL-6 in nude mice
 - decreases viral replication
- DCP and Calcium Pterin
 - suppress indoleamine (2,3)-dioxygenase (IDO)





And...More Cancer Targets for DCP Based on IL-12 Up-Regulation

- **Metastatic melanoma**
- **Metastatic renal cell cancer**



Reference: Weiss JM, Subleski JJ, Wigginton JM, Wilttrout RH. Immunotherapy of cancer by IL-12-based cytokine combinations. *Expert Opin Biol Ther.* 2007 Nov;7(11):1705-21.



Competition

- No approved products in this category (IDO Modulators) - First in class
- Xeloda is one of the few oral products used in Breast Cancer, but w/ 15-28% effectiveness¹
- SERMs e.g., Tamoxifen (oral); only effective in treating estrogen receptor-positive breast cancers and tumors develop resistance.²
- Estrogen receptor down-regulators e.g., Faslodex®
- Chemically block ovarian estrogen (Lupron®, Zoladex®)
- Aromatase inhibitors (Femara®, Arimidex®, Aromasin®)
- National Cancer Institute is also testing the IDO competitive inhibitor L-Methyl-d-Tryptophan
- Various cytotoxic compounds
- Our goal is to partner with Big Pharma, not compete
- We are different because we are oral and without cytotoxic side-effects like hair-loss and nausea

Company Traction

- Issued and pending patents filed
- Experienced scientific and business team
- Strong scientific advisors
- Internationally renowned scientific collaborators
- Key [scientific publications](#)





Scientific Advisors

Phillip B.B. Moheno PhD – Chief Scientist, SanRx

Dietmar Fuchs PhD – Medical Chemistry, Innsbruck Medical University, Austria

Boris Minev MD – Assoc. Research Scientist, UCSD Moores Cancer Center

James C. Ryan PhD - UC San Francisco, Immunology

Wolfgang Pfeleiderer PhD – Prof. of Chemistry, Univ. of Stuttgart and Konstanz in Germany

Vincent Gammill ScD – Director, Center for the Study of Natural Oncology

Christiana Winkler PhD - Innsbruck Medical University (Austria), Medical Chemistry

Katharina Schroecksadel PhD - Innsbruck Medical University (Austria)

Arnold L. Rheingold PhD - UC San Diego, Chemistry & Biochemistry

Antonio G. DiPasquale PhD - UC Berkeley, Chemistry

Ana Maria Barral PhD – SanRx Consultant

John D. Morrey PhD - Institute for Antiviral Research, Utah State University

Daniel F. Hoft MD PhD – Saint Louis Univ., Immunobiology, Internal Medicine, & Microbiology

Isaac Sakala PhD - Saint Louis Univ., Immunobiology, Internal Medicine, & Microbiology

Svetlana Nikoulina PhD – Director of Preclinical Research & Development, SanRx



Summary

- Calcium pterins are oral, non-toxic immune modulators
- IP covers calcium pterins' compositions of matter
- Mechanism of Action studies suggest compound modulates IDO, a known target
- Numerous large market opportunities
- Management team and advisors established
- Seeking funding to develop Pterin+Calcium as a dietary-supplement and DCP as a pharmaceutical

