

Opportunity Concerning Vitamin D Metabolites for Osteoporosis, Dermatology & Other Indications

This is a unique opportunity to form a partnership with Herbonis AG for the development and commercialization of plant-based products for the prevention and treatment of osteoporosis and other diseases in humans.

The partner will gain access to:

- The expertise of Herbonis and its network of leading scientists
- the results of work carried out to date, including research into efficacy of vitamin D metabolites, know-how for the breeding and cultivation of suitable plants and process development work for extraction, purification and formulation.
- world-wide marketing rights for a product that, once approved, will enter a substantial market.

Opportunity: Herbonis is looking for a partner to support further development work and clinical trials for therapeutic products derived from plants producing vitamin D-metabolites. Namely, *trisetum flavescens* (TF) and *solanum glaucophyllum* (SG). The expected indications are currently osteoporosis and dermatology.

In return, the partner will receive marketing rights for products successfully developed from this work.

Cultivation trials have succeeded in obtaining economical yields. The feasibility of the production method has been demonstrated. Efficacy has been demonstrated in chickens, and this has led to the first sales to a feed marketing partner.

Herbonis AG: A Swiss company founded in 2001 by scientists retired from F. Hoffmann – La Roche Inc., Herbonis has laboratories located near Basel. It also has a strategic alliance with www.vitaplant.ch for plant development.

With a network of world-class scientists, Herbonis specializes in the development and production of plant-based products for the treatment and prevention of bone diseases in animals and humans.

Osteoporosis

Osteoporosis is currently treated with bisphosphonates and other products aimed at slowing bone resorption. The greatest unmet need, however, is for an agent that can actually stimulate the formation of new bone.

Herbonis believes that vitamin D₃ metabolites are ideal compounds to effectively fill this need.

Vitamin D Designations

(i) Vitamin D:

- Vitamin D₂ Ergocalciferol
- Vitamin D₃ Cholecalciferol

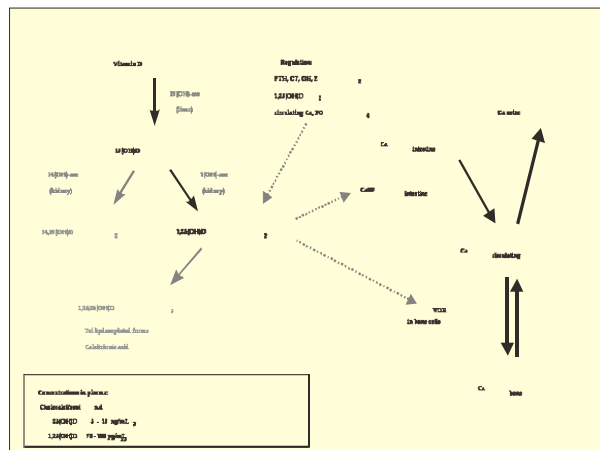
(ii) Vitamin D-Metabolites (VDM):

Natural formation in humans and animals as active compounds exerting the biological action of vitamin D: (25(OH)D, 1,25(OH)₂D and others. However, in various conditions too little metabolites are formed and need to be supplied additionally.

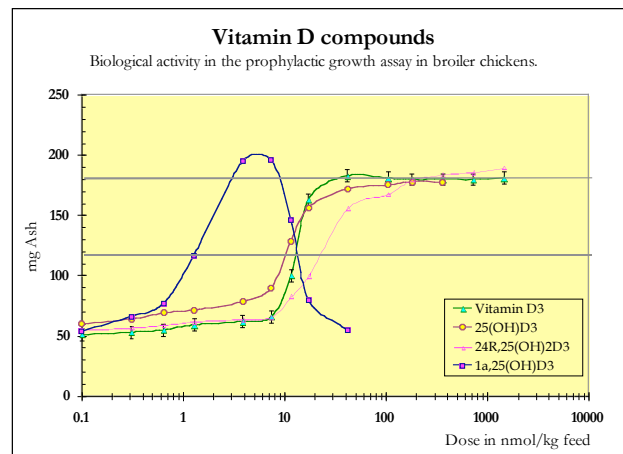
(iii) Vitamin D-Derivatives:

Unnatural, synthetic compounds designed as drugs: 1α(OH)D, Calcipotriol.

Vitamin D Metabolism



Calcitriol (CTL) is the Most Active Metabolite



Vitamin D Metabolites from Plants

(i) *Solanum glaucophyllum* (malacoxylon)

- native to South America
- active principle: mixture of cholecalciferol, 25 (OH) D₃ and 1,25(OH)₂ D₃ and their glycosides = vitamin D-metabolites (VDM)
- contents: 0.1 to 120 mg/kg dry matter (selection and breeding program underway)

(ii) *Trisetum flavescens* (Golden Oat)

- native to pre-alpine pastures
- active principle: similar mixture of vitamin D-Metabolites as above
- contents less than 0.1 mg/kg dry matter
- improvement potential high (selection and breeding program underway)

Breeding and cultivation of plants

Increasing the contents of vitamin D-metabolites by:

- Breeding of *Trisetum flavescens*
- Breeding of *Solanum glaucophyllum*
- Optimisation of *Trisetum flavescens*
- Cultivation of *Solanum glaucophyllum*
- Coordination of worldwide trials and cultivation
- Production of *Solanum glaucophyllum* active substance

Highlights of Plant Development

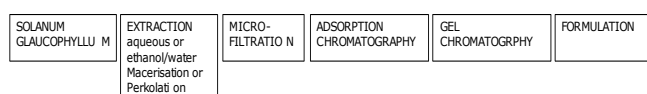
Increasing levels of active components:

- Successful selection of plants with high CTL contents
- Higher CTL-yields by applying agronomic measures
- Test plots in various locations on both hemispheres

Process Development

Several extraction and purification methods are being explored. Final process depends on marketing partner or contract manufacturing facilities. A feasible process will follow the scheme depicted below:

VDM-CONCENTRATE FROM *SOLANUM GLAUCOPHYLLUM*



From a wild species to a cultivated plant with a high content of VDM

technical ly feasible process

Vitaplant
Plant development
Logistics

HEVs Sion
partly sponsored by KTI

no activities

Extraction, Filtration and Concentration

Step 1 EXTRACTION and FILTRATION

Step 2 MICROFILTRATION and CONCENTRATION

Step 3 CHROMATOGRAPHY and CONCENTRATION

The structure of the main component, a CTL-glycoside, has been elucidated and filed for patent application.

Products for Animal Markets

(i) Animal Nutritional Product (PAM-Herbal Vitamin D)

Description: Minimally standardized SG product 10 ppm
 Marketer: www.pancosma.com
 Registration: Switzerland in progress; EU notification
 Efficacy: Demonstrated
 Safety: Pilot Study showed wide range of safety

(ii) Animal Health Product (Solbone-Pure)

Description: Standardized, characterized SG product > 500 ppm
 Marketer: Open
 Registration: EU Notification
 Efficacy: Demonstrated
 Safety: Pilot Study showed wide range of safety

Products for Human Markets

(i) Human Health Product (Solbone Pharma Quality)

Description: Highly purified, standardized and characterized SG product
 Marketer: Open
 Registration: Open
 Efficacy: pre-clinical model of Osteoporosis in process
 Safety: Study in 2004/5

(ii) Human Nutrition Product (Trisbone)

Raw material: *Trisetum flavescens* cultivation and extraction
 Description: Minimally standardized extract >50 IUD/g
 Marketer: Open
 Registration: Open (for food/OTC as herbal VD product)
 Efficacy: To be shown in a pre-clinical model of osteoporosis (2004)
 Safety: Study in 2004/5

Biology: Next steps

2 studies have demonstrated efficacy in animal health. The next steps are:

(i) Biological Testing in Dermatology

Collaboration: www.pentapharm.com

Test: Exploration of SG and TF extracts in in-vitro models of cell differentiation

Status: Under discussion

(ii) Biological testing in Osteoporosis

Collaboration: Open

Test: Exploration of SG and TF extracts in a preclinical rat model for osteoporosis in progress

Status: Under discussion

Main Achievements

Parallel development of main tasks:

- Wild plant propagated agronomically
- Analysis, extraction and purification
- Efficacy demonstrated in target animal
- Comprehensive patent application filed
- First sales to feed marketing partner

Herbonis Business Case

Elaboration of important USPs

- Vitamin D-metabolites play key role in bone formation
- Natural metabolites offer safe therapeutic window (patent application)
- Products offer favourable application properties
- Efficacy in target animals proven
- Effects shown in cell cultures relevant for dermatology
- First economical product in feed market
- Patent pending for use in humans and animals
- Registration of productive plant strains planned
- Trade secrets for agronomy and analytics elaborated

Competitive advantages include:

- Natural, bone-forming substance
- Natural products enjoy consumer acceptance
- Products not reproducible by synthesis
- Proprietary plant strains
- Proprietary plant agronomy
- Proprietary analytics
- Piloted extraction and purification
- Patentable processes, products and use
- Experienced management team
- Expert network

Herbonis revenue model

1. Sale of substance (for pharma, food, cosmetics, feed markets)
2. License income from patents and brands

Next Steps

If you have further questions regarding this opportunity, or would like to open discussions, please contact:

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Herbonis Business Model

