

# *Hoodia gordonii* as a functional food ingredient

October 2009



**Vital Solutions.**



# Content of presentation



## ✿ Who are we?

- Introductions to Phytopharm, PhytoTrade Africa and Vital Solutions

## ✿ What has changed in the last 12 months?

- History of previous development collaborations by Phytopharm

## ✿ Why are we still interested in Hoodia?

## ✿ What are the key tasks and investment required?

## ✿ Programme status and collaboration

## ✿ Next R&D steps

- Evaluation of existing scientific data
- Determination of new potential actives
- Proving weight loss efficacy

## ✿ Publications

## ✿ Product development / Food Formulations

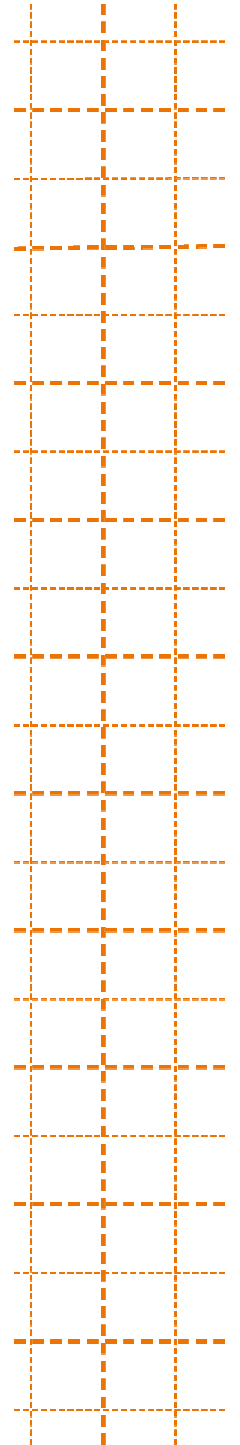
## ✿ Regulatory approvals

## ✿ Concluding comments

# Who are we?



**Vital Solutions.**



# Project partner - Phytopharm plc

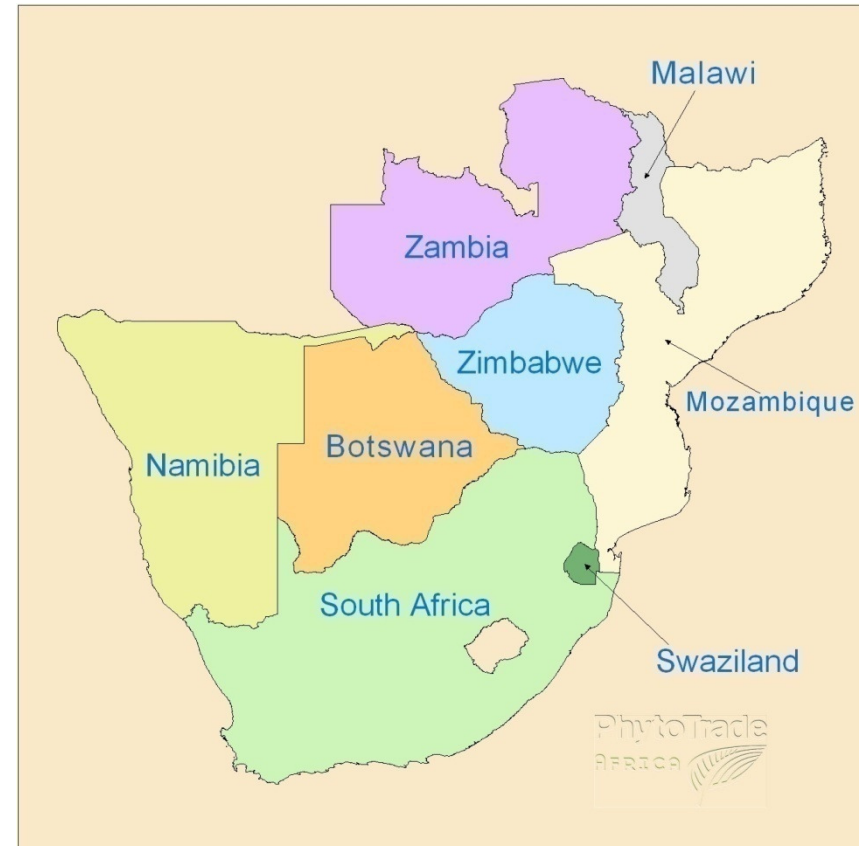
---



- Phytopharm plc (PYM), is a **pharmaceutical** and **functional food** development company based in the UK. Our products are developed from medicinal plants
- PYM is listed on the London Stock Exchange market since 1996. Funding for our research and development programmes is mainly from investment funds
- Our key programmes:
  - **Pharmaceutical**: Cogane™ for Parkinson's Disease
  - **Pharmaceutical**: Myogane™ for Motor Neurone Disease
  - **Functional foods**: Hoodia extract for weight management
  - **Functional foods**: Phytopica®, a veterinary product for canine skin health
- PYM first licensed the rights to commercialise Hoodia from the CSIR in 1998. We have worked in joint collaborations with Pfizer Inc. (as a **pharmaceutical**) and Unilever (as a **functional food**). The collaboration with Unilever ended in Dec 2008

## Project partner - PhytoTrade Africa

- Non-profit trade association representing 58 members
- SME's, producer groups, NGO's, researchers, other groups) in 8 countries
- Focus only on indigenous plants
- Launched in 2001
- Member of Union for Ethical Biotrade, ABS central to our work



## Project partner - PhytoTrade Africa

---

- Objective – develop income for rural producers
- Develop and facilitate large and sustainable markets
- Facilitate economic development in Southern Africa
- Technology transfer
- Partnership approach



# Project partner - Vital Solutions GmbH

---

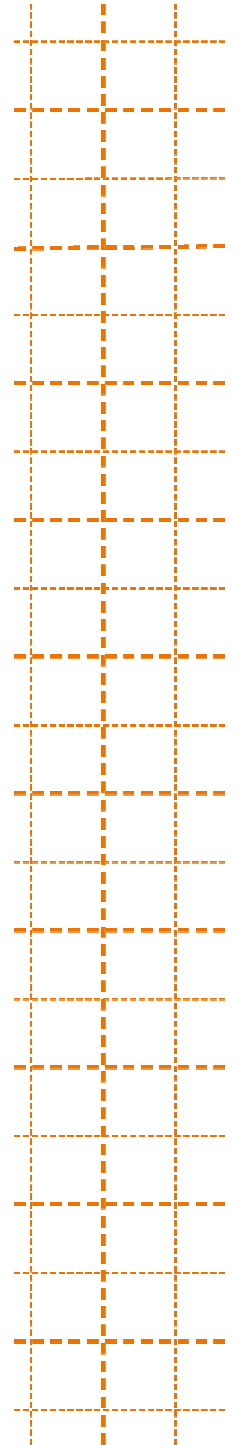
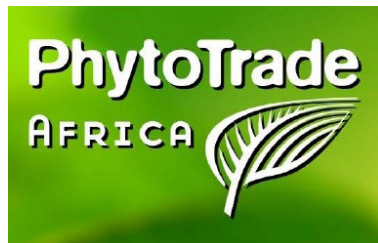


- ✿ Vital Solutions works globally in the field of natural ingredients for use in food, dietary supplements and cosmetics
- ✿ Business areas are:
  - New product development & supply chain
  - Sales and marketing of natural products
  - Consulting of B2B and B2C Companies
- ✿ Vital Solutions was founded in June 2009. Its headquarters are in Düsseldorf, Germany
- ✿ Vital Solutions has a strategic partnership with PhytoTrade Africa to focus on new product developments in Southern African countries. The aim is to evaluate additional applications for traditionally used food plants that have sufficient supply capacity.

# History of previous collaborations



**Vital Solutions.**





# An overview: history of collaboration to 2003

---

- ✿ *Hoodia* plants have been utilised as a food and water source by indigenous peoples of southern Africa; written use dates back to 19<sup>th</sup>C
- ✿ 1960s: the CSIR (Council for Scientific and Industrial Research) observed the appetite suppressant affects of *Hoodia* in the laboratory
- ✿ 1996: the CSIR patented the use of products derived from *Hoodia* as an appetite suppressant (PCT patent WO98/46243; x2 US patents)
- ✿ 1997: the CSIR licensed the Patent rights for the commercialisation of *Hoodia* to Phytopharm (PYM)
- ✿ 1998: PYM entered into a licensing agreement with Pfizer Inc. for the development of a prescription pharmaceutical for obesity
- ✿ 2003: the CSIR and the San Council signed a Benefit Sharing Agreement
- ✿ 2003: Pfizer Inc. closed their Natureceuticals group, discontinued clinical development and returned the rights to PYM

# An overview: history of collaboration 2004 - 2008

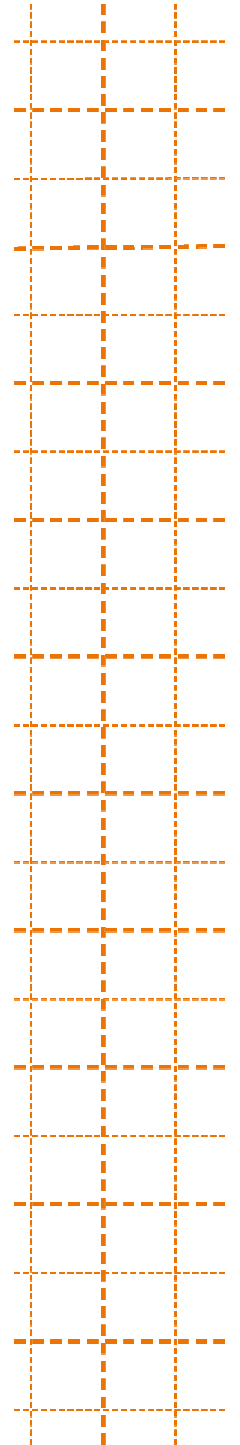
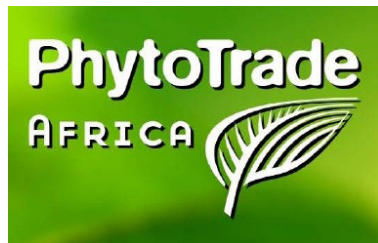
---

- ✿ Dec 2004: PYM entered into a Joint Development Agreement with Unilever, to develop *H. gordonii* extract as a functional food ingredient with clinically proven efficacy
- ✿ From 2005, the joint collaboration focused on:
  - ✿ Development of an extraction process to produce *H. gordonii* purified extract to a defined specification
  - ✿ A science programme to complete further non-clinical work and 4 clinical trials
  - ✿ Ramping up a substantial supply chain for cultivated plant material
- ✿ Dec 2008: Unilever withdrew from the programme and terms were agreed in a Mutual Termination Agreement with PYM:
  - ✿ All original patent rights returned to PYM. Unilever granted PYM a non-exclusive, perpetual, irrevocable, worldwide royalty-free license, with the right to sub-license, to any Unilever patents, IP rights and know-how connected with the Hoodia programme

# Why are we still interested in Hoodia?



**Vital Solutions.**



# Commercial targets

---

Phytopharm plc	PhytoTrade Africa	Vital Solutions GmbH
<p>To secure a new licensee.</p> <p>To market <i>H. gordonii</i> extract for weight management in functional food applications in US and European markets.</p> <p>Phytopharm is also exploring other opportunities including dietary supplements and phytomedicines.</p>	<p>To contribute to viable supply chains and successful commercialisation of Hoodia</p>	<p>To develop <i>H. gordonii</i> standardised extract as a functional food, dietary supplement or cosmetic ingredient globally, focusing on US first.</p> <p>To ensure that ABS-compliant investments made in the supply chain and in the scientific programme, materialise into value-added products, originating from Southern Africa</p>

# Markets

---

## Obesity

Obesity is no longer an image and vanity related issue, as clinical trials have clearly established its connection with other diseases. This includes an accelerated onset of diabetes and cardiovascular disease.

The World Health Organization (WHO) predicts that there will be more than 1.5 billion obese people globally by 2015.

According to the International Association for the Study of Obesity (IASO), the UK has the highest percentage of obese adults (62.2 per cent), followed by Germany and Spain where over 50 per cent of the population is overweight.

## Weight loss market

Marketdata estimates that the total U.S. weight loss market was worth \$55.4 billion in 2006. The market should reach \$58.7 billion this year and \$68.7 bill. by 2010.

Current market leaders are Weight Watchers (\$1.2 bill.), NutriSystem (\$568 mill.), LA Weight Loss (\$500 mill.), Jenny Craig (\$462 mill.)

# Consumer demand

---

America's estimated 72 million dieters - about 70% of whom try to lose weight by themselves, are moving from one diet to another desperately searching for the magic formula or plan that makes weight loss effortless.

Consumers say that the main reason why diets are not successful or why it is not possible to maintain the reduced body weight after the diet, is the hunger and appetite which force them to eat uncontrollably.

Based on this experience, recently launched ingredients or ingredients which will be launched soon are targeting appetite reduction as effect for the food product.

Due to recession in 2009, less growth was shown. Dieters shifted to less costly retail and do-it-yourself options such as: meal replacements, OTC diet pills, mail order plans, diet websites, and fad diet books.

In addition, there will be competition from at least one and probably several new prescription diet drugs that are likely to be approved for sale in the U.S.

# Example of food ingredients for weight management

---

<b>Current ingredients</b>	<b>Effects</b>
CLA (conjugated linoleic acid)	Reduction of fat mass and induction of lean body mass
Protein Isolates	Appetite suppressant
Oligofructose	Appetite suppressant
Pinoleic acid	Appetite suppressant
Citrus aurantium (Bitter orange)	Thermogenic properties which increase conversion of calories to heat
Cammelia sinensis (Green tea)	Thermogenic properties which increase conversion of calories to heat
<b>New ingredients to be used soon</b>	
Caralluma fimbriata	Appetite suppressant
Simmondsia chinensis (Jojoba)	Appetite suppressant

# Example of drugs for weight management

---

- US, Europe and Japan combined market: \$600M (2005) to \$2B (2010)  
AP, Espicom Healthcare Intelligence report, 2007

	<b>Company</b>	<b>Brand/ID</b>	<b>Target</b>	<b>Advance</b>
Available	Roche	Xenical	Lipase	
	Abbott	Meridia	Serotonin uptake	
	Glaxo	Alli (otc)	Lipase	
	Sanofi	Acomplia	CB1 receptor	Europe only
Off-label	Amylin	Byetta	Incretin-like	
		Symmlin	Amylin-like	
Pipeline	Pfizer/BMS	PF-04415060	DGAT-1 inhibitor	Preclin
	Orexigen	Empathic	Antidepressant	Phase II
	Novo Nordisk	Liraglutide	GLP-1-like	Phase II
	Merck	Taranabant	CB1 receptor	Phase III
	Arena	Lorcaserin	HT2C stimulation	Phase III
	Vivus	Qnexa	Serotonin release	Phase II
	Dibex	DIO-902	Cortisol inhibitor	Phase II



# What does *H. gordonii* need to get to market?

---

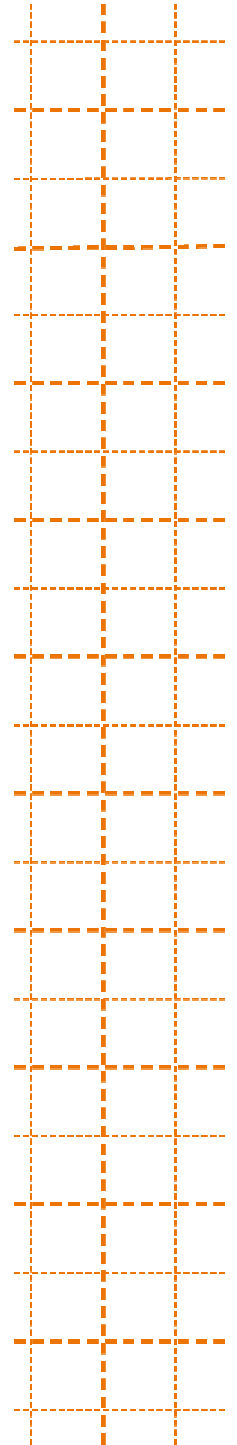
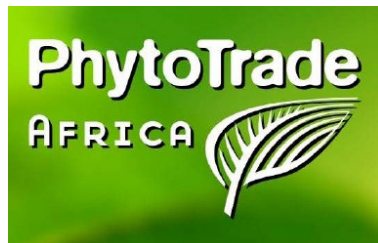
- ✿ Scientifically proven to deliver weight loss benefits safely
- ✿ Only then can a product(s) have the scientific claims to successfully out-compete products already in the international market (some of which are fraudulent)
- ✿ This will require a co-ordinated effort by all parties including:
  - ✿ All Hoodia stakeholders
  - ✿ PYM, PTA, VS and CSIR to guide the scientific programme
- ✿ Securing funding is absolutely necessary if we are to take the programme forward:
  - ✿ PYM is seeking a new licensee
  - ✿ Additional donor funding is also required

- 
- ✿ Potential to identify new, additional constituents
  - ✿ And evaluation of their alternative applications
-

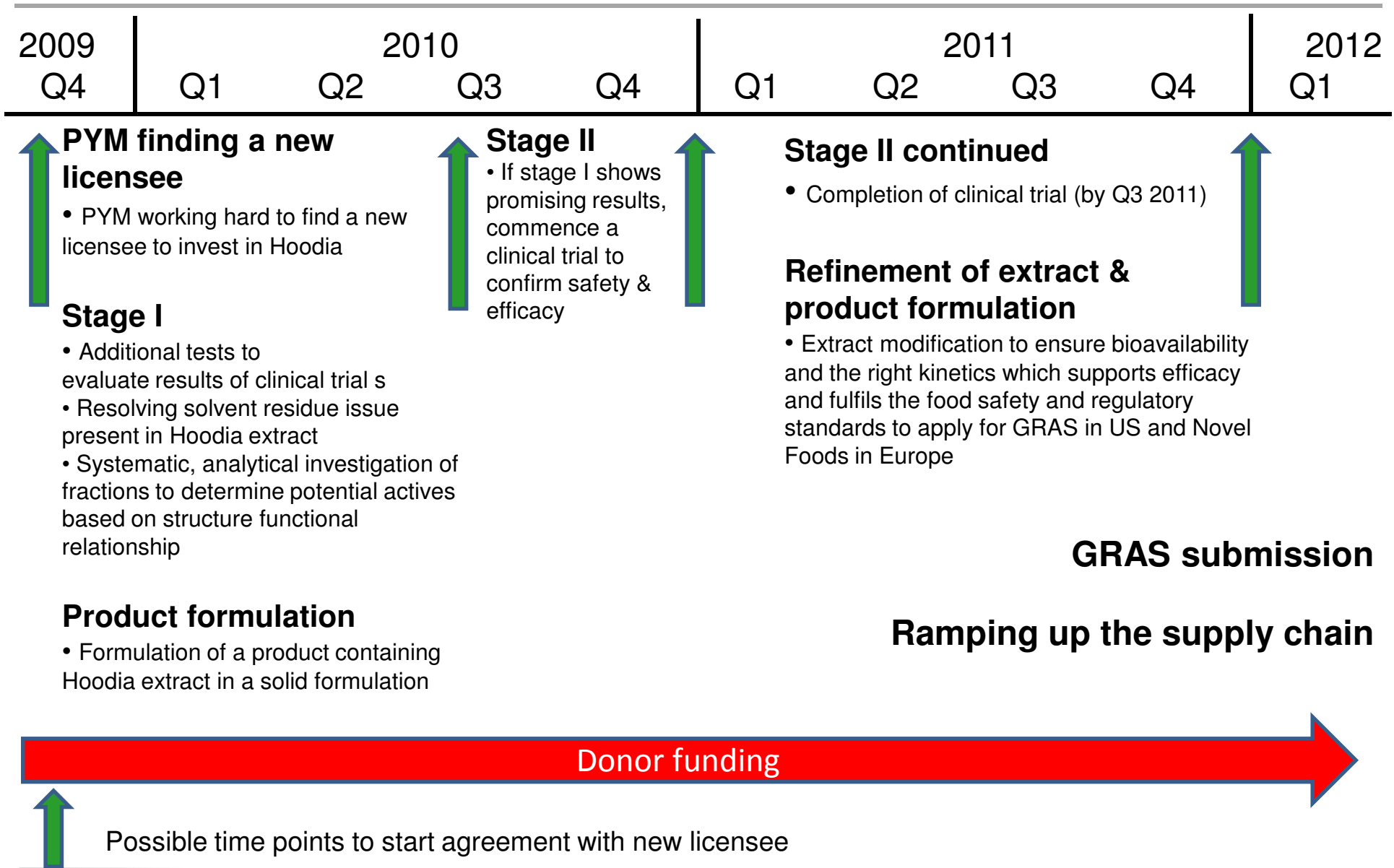
# What are the key tasks and investment required?



**Vital Solutions.**



# Development timing and potential financing



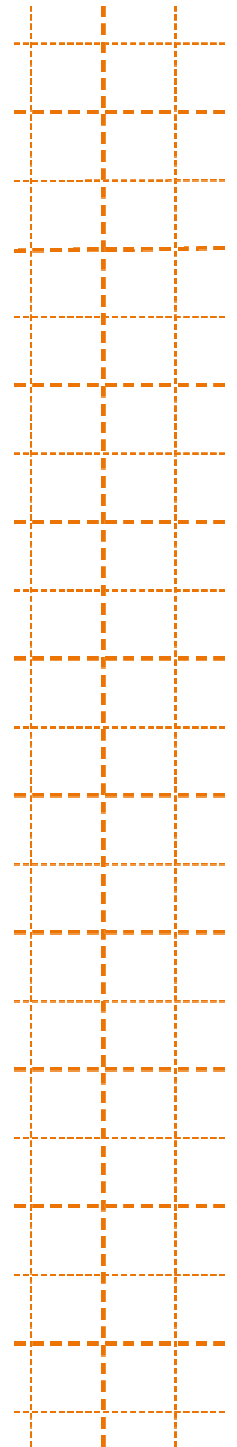
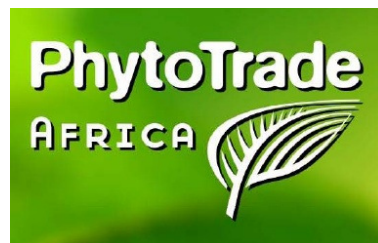
## Development - through private public partnership

Development area	Topic	Donor
<b>Raw material</b>	Cultivation Drying Milling	Supporting agricultural development
<b>Extraction process</b> Drying to target powder extract	Residual solvent levels Drying technique	Supporting innovative technologies
<b>Clinical Science</b> weight management	Efficacy & Safety Proof of concept program Human studies	Supporting clinical research, human science
<b>Applications</b>	Cereals, bars	Supporting development of consumer products
<b>R&amp;D</b> to identify other Hoodia compounds as potential food ingredients	Other applications, use of by-products /waste fractions	Supporting innovations and the development of new ingredients
<b>Regulatory</b>	GRAS approval, Novel food notification, health claims	Supporting developing countries to have access to markets by overcoming regulatory hurdles
<b>Institutional &amp; industrial alliances</b>	Skills and knowledge transfer	Supporting industrial development

# Programme status and collaboration



**Vital Solutions.**



# Programme status

---

- ✿ Since 1997, the programme has seen the development of 4 types of *H. gordonii* extracts; these have been required at different stages of the joint development programmes (with Pfizer and Unilever)
- ✿ Numerous *in vitro*, *in vivo* and clinical investigations have been completed with these extracts in order to demonstrate their efficacy and safety
- ✿ Although a large body of data have been gathered, additional work on the efficacy and safety is still required
- ✿ Understanding and interpretation of the results from a 15 day clinical study in females is ongoing
- ✿ Immediately after the 15 day clinical study, Unilever concluded that *H. gordonii* extract was not suitable for a Unilever-branded beverage product
- ✿ Additional work is required to answer open questions that remain in the science programme prior to achieving EU Novel Food and FDA GRAS notification

# Current supply chain and Investment to maintain capacity

---

- ✿ PYM has retained a proportion of the supply chain that was established under the Unilever joint partnership. This includes:
  - ✿ Plants under cultivation at two farm sites in South Africa and Namibia
  - ✿ Dried *H. gordonii* stocks in storage in South Africa and Europe
  - ✿ Significant quantities of *H. gordonii* seeds in long-term cold storage, sufficient for the cultivation of hundreds of hectares



# Hoodia project plan proposal

	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	
<b>Actions</b>	<b>2009</b>						<b>2010</b>												<b>2011</b>												
Securing donor funding																															
Securing a new licensees																															
Publication of journal supplement																															
IMD (bio profiling)																															
Solvent residues: regulatory, safety assessment																															
Solvent residues: analytics & process																															
Production PYM50717 for clinical trial																															
Formulation and stability																															
Safety testing ( <i>in vitro</i> ) for PYM50717 (for stage 1)																															
Business plan, investor presentations																															
Drying raw material																															
Process development for newly identified fraction (s)																															
Safety, efficacy test programme for new extract (s)																															
Clinical trial on PYM50717																															
GRAS dossier preparation & submission																															
Clinical trial on new extract(s)																															
Supply chain integration (pilot drying plant / farmer contracts)																															

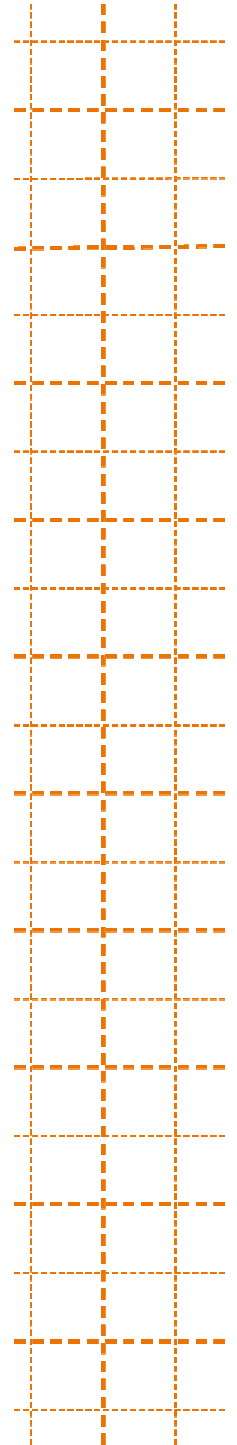
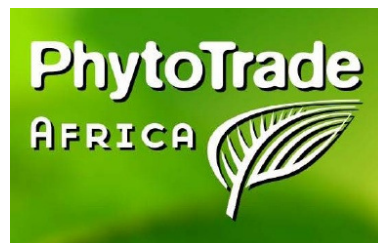


## Next R&D steps

- Evaluation of existing scientific data
- Evaluation of side stream opportunities
- Proving weight loss efficacy



**Vital Solutions.**



# Evaluation of existing scientific data

---

The available data suggests that additional tests need to be carried out in order to fully understand their meaning.

Tests would include receptor binding assays as well as an additional evaluation of metabolic functions.

- ✿ The total estimated cost for this evaluation is estimated to be € 300.000 (ZAR 3 million)
- ✿ Necessary time period would be 3-4 months



It is highly recommended to complete these test before starting any further clinical study for weight management.

# Identification of other potential side stream products

---

- The Hoodia extract developed (with Unilever) is a purified extract containing >75% active ingredients. The total yield from raw material to extract is ~1%. Which indicates that 99% of the plant material is currently considered as waste.
- The intention is to look into side streams of the current process to identify other potential applications.
- Highly innovative techniques available within the network of Vital Solutions would enable the identification of compounds (structure elucidation) and their evaluation against known molecular structures within a proprietary database.
- Prediction of activities and toxicity is therefore possible.
- The aim is to identify one or more potentially safe fraction(s), that are easy to extract and might have an interesting activity to serve consumer demands.

# Weight loss efficacy

---

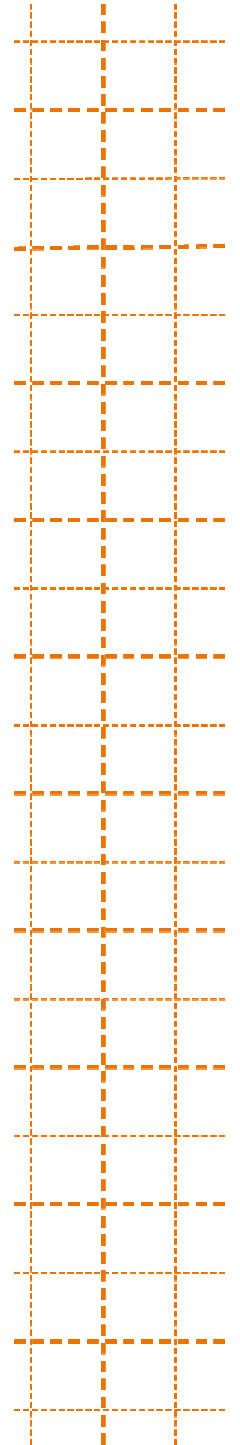
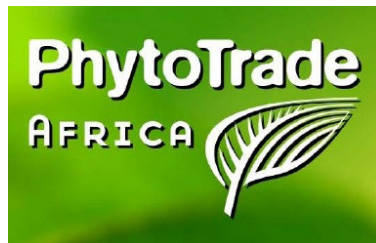
To prove weight loss efficacy, it is envisaged that the following is required:

- ✿ A single dose study in overweight / obese target population to test:
  - ✿ Safety and tolerability
  - ✿ Evaluation of the kinetics of the solid formulation
  - ✿ Estimated cost: £80,000 (ZAR 1 million)
- ✿ A 90 day repeat dose study in overweight / obese target population:
  - ✿ A scientific advisory panel is to design the study
  - ✿ Placebo controlled
  - ✿ Safety, tolerability and kinetics need to be addressed
  - ✿ Estimated cost: not known
- ✿ Primary endpoint: weight loss
- ✿ Suggested secondary endpoints: changes in body fat % and distribution, BMI, waist measurement, cholesterol, insulin, glucose

# Publications



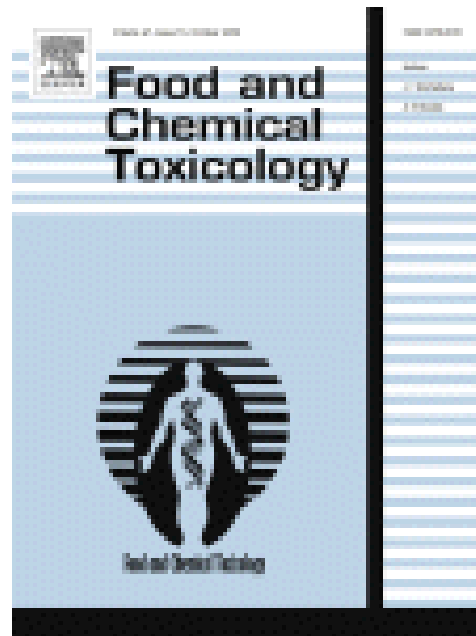
**Vital Solutions.**



# Publications to support GRAS designation

---

- Unilever and PYM aim to publish a series of 8 articles as a supplement to the Journal of Food and Chemical Toxicology, to support GRAS designation. Target date: Q1 2010

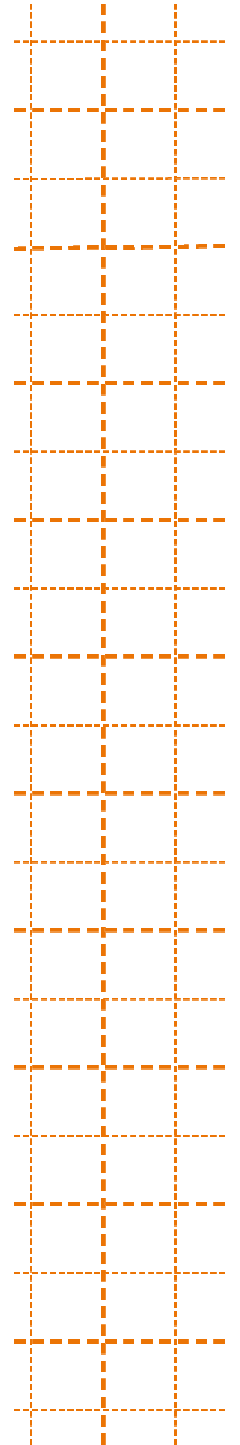
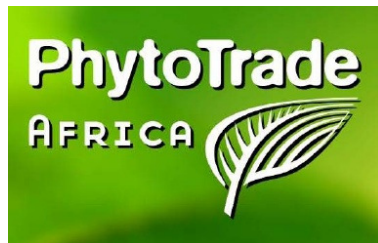


- Other publications are in progress as joint publications between Unilever and PYM; this will include the publishing of the results from the 15 day clinical study. Target date: Q2/Q3 2010

# Product development



**Vital Solutions.**



# Prototype products

---

- ❁ Previous clinical studies have utilised four different *H. gordonii* extracts in a mixture of capsule and liquid formulations
- ❁ In recent months, PYM has completed product formulation work, adding *H. gordonii* purified extract (as a powder) into solid formulations:
  - ❁ Mango, orange, lime and cashew nuts cereal bar
  - ❁ Mixed berries and flaked almonds cereal bar
  - ❁ Fruit and nut cereal mini-bites

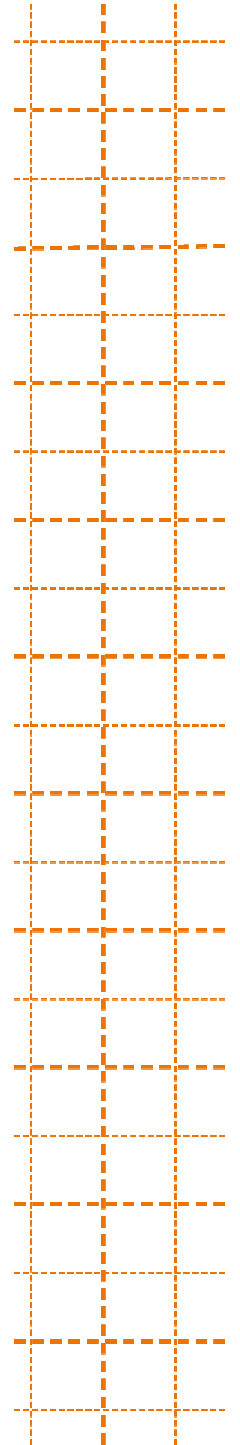
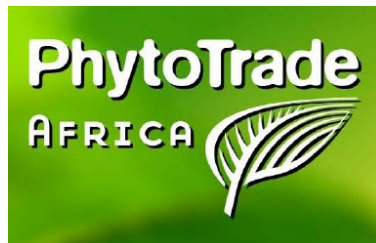




# Regulatory approvals



**Vital Solutions.**



# Regulatory approval – weight management

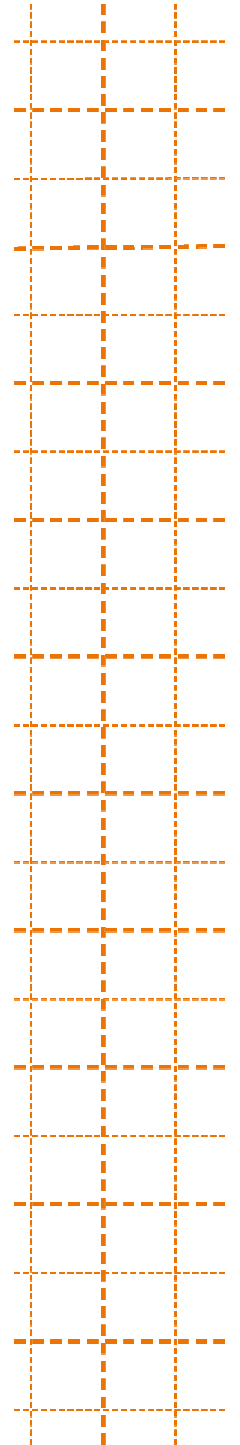
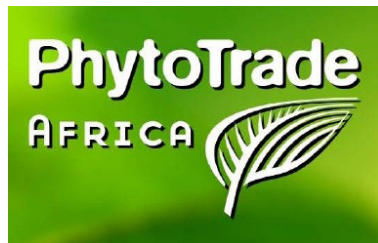
Europe		USA	
Step 1: Approval to be used in foods and food supplements as a safe ingredient			
Novel food approval		GRAS + DSHEA	
Estimated costs for safety studies ~ € 250.000 + GMP ~€ 200.000			
18-36 months*	~€ 500.000, if all data is available	12 months*	~€400.000, if all data is available and process / production facility is GMP status confirmed
Step 2: Approved health claim			
EFSA 13.5 approved health claim		FDA approved health claim	
12-15 months*	~€300.000, if all data is available and dossier is ready	12 months*	~€200.000, if all data is available and dossier is ready
Estimated clinical study costs ~€ 1.5 milion			

\* Estimated time based on experience; each ingredient has individual time-frames

# Concluding comments



**Vital Solutions.**



# Concluding comments

---

- ✿ The Hoodia stakeholders and PYM / CSIR / VS / PTA need to co-ordinate all our efforts to pull in the same direction
- ✿ Without scientific evidence to support weight loss, there is no market for Hoodia as a functional food in major economies. Any product will need scientific claims
- ✿ However, there are several drugs and weight management functional foods on the market and others in the pipeline, so time is not on our side  
Funding is urgently needed
- ✿ Without this, small companies like VS / PTA / PYM cannot continue to finance the development programme. We need help from governments also.