

# apitope

Therapeutics to Halt Autoimmune Disease Progression

Corporate Presentation, May 2010

Dr Keith Martin, CEO

# Apitope Mission

Become the leading peptide therapy company for  
autoimmune diseases

Partner of choice for pharmaceutical companies keen  
to develop disease modifiers for autoimmune  
conditions

# Apitope in Summary

- European biotech company developing therapeutic peptides for treating autoimmune and allergic diseases
- Revolutionary disease modifying therapies that selectively treat the underlying cause of a range of diseases
- Leading edge, high speed apitope™ discovery platform for peptide therapeutics (**A**ntigen **P**rocessing **I**ndependent **e**pi**T**OPE)
- Lead product candidate for Multiple Sclerosis partnered with Merck Serono in Phase I development
- Innovative pipeline includes
  - Pre-product candidate to prevent factor VIII induced inhibitor antibodies
  - Two new discovery programmes initiated in MS partnered with Merck Serono
  - Three further discovery targets
- Experienced management team backed by strong investor base

# Investors

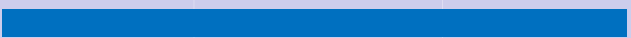
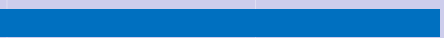

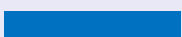

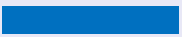



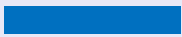



- Series B: €10 million + up to \$1 million



# Business Strategy

- **Focus on areas of opportunity and expertise**
  - Conditions where unmet needs are high
  - Internationally recognised experts at Apitope
  - Established track record of successful product development
- **Balance portfolio**
  - Therapeutic targets with early proof of concept
  - Early revenue opportunities through partnering
- **Development efficiency**
  - Currently discovery in house and development out sourced to CROs with strong in house management
- **Partner to capture value**
  - Proof of Concept in man (Phase II) for maximum investment return

# R&D Pipeline: Current Status and 2012 Targets

Project	Indication	Partner	Discovery	Preclinical Development	Phase I Safety	Phase I PoP	Phase II
ATX-MS-1467	Multiple Sclerosis	Merck Serono					
ATX-MS2	Multiple Sclerosis	Merck Serono					
ATX-MS3	Multiple Sclerosis	Merck Serono					
ATX-F8	Factor VIII intolerance						
ATX-GD	Graves disease						
Project 2	Undisclosed						
Project 3	Undisclosed						

# Apitope Corporate Structure

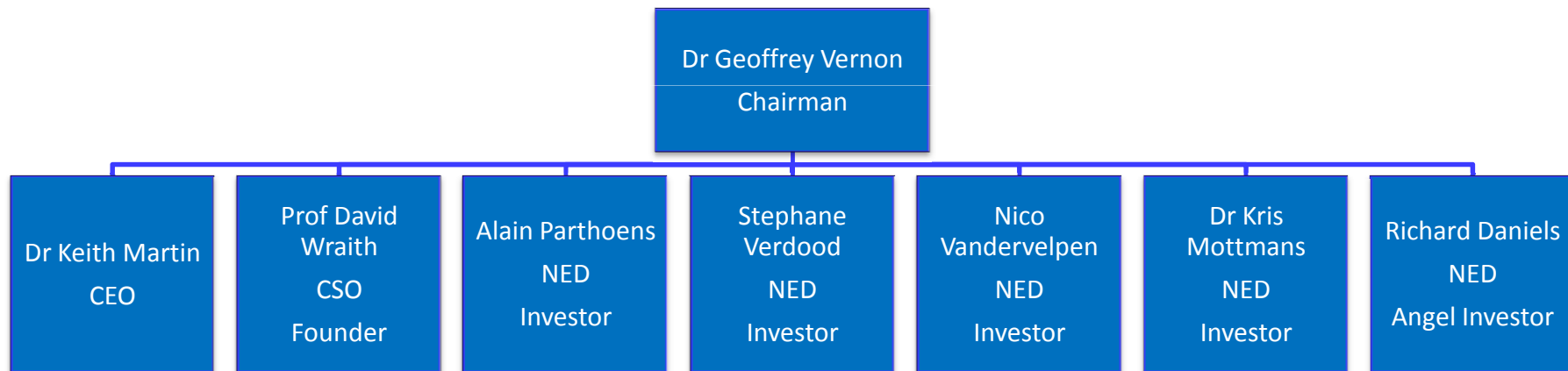
Apitope  
International NV

Located in Hasselt  
Corporate HQ

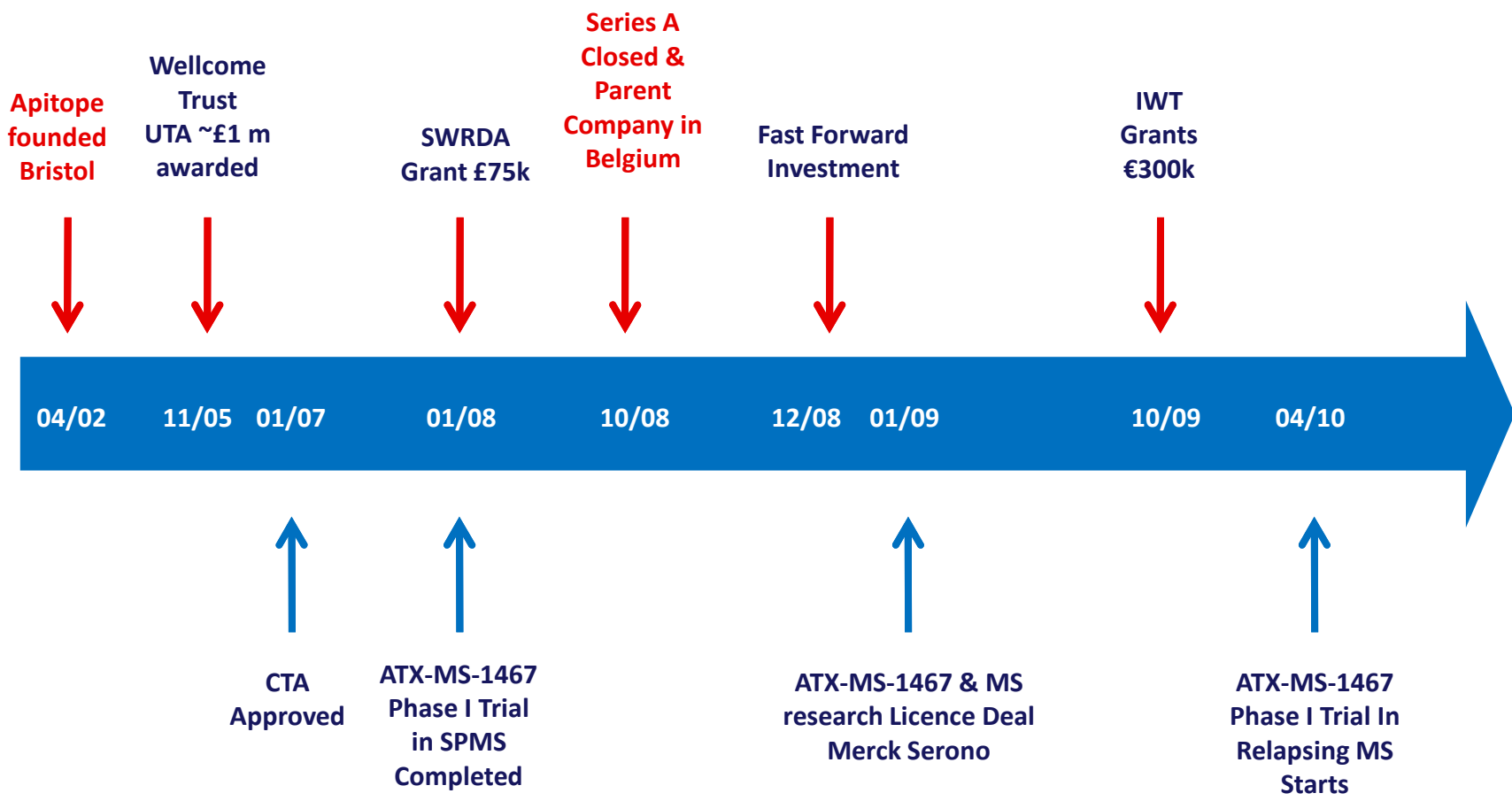
Apitope Technology  
(Bristol) Ltd

Wholly owned subsidiary  
Located in Bristol

# Apitope International NV: Board of Directors



# Strong Track Record



# Clinical Problem and Apitope Solution

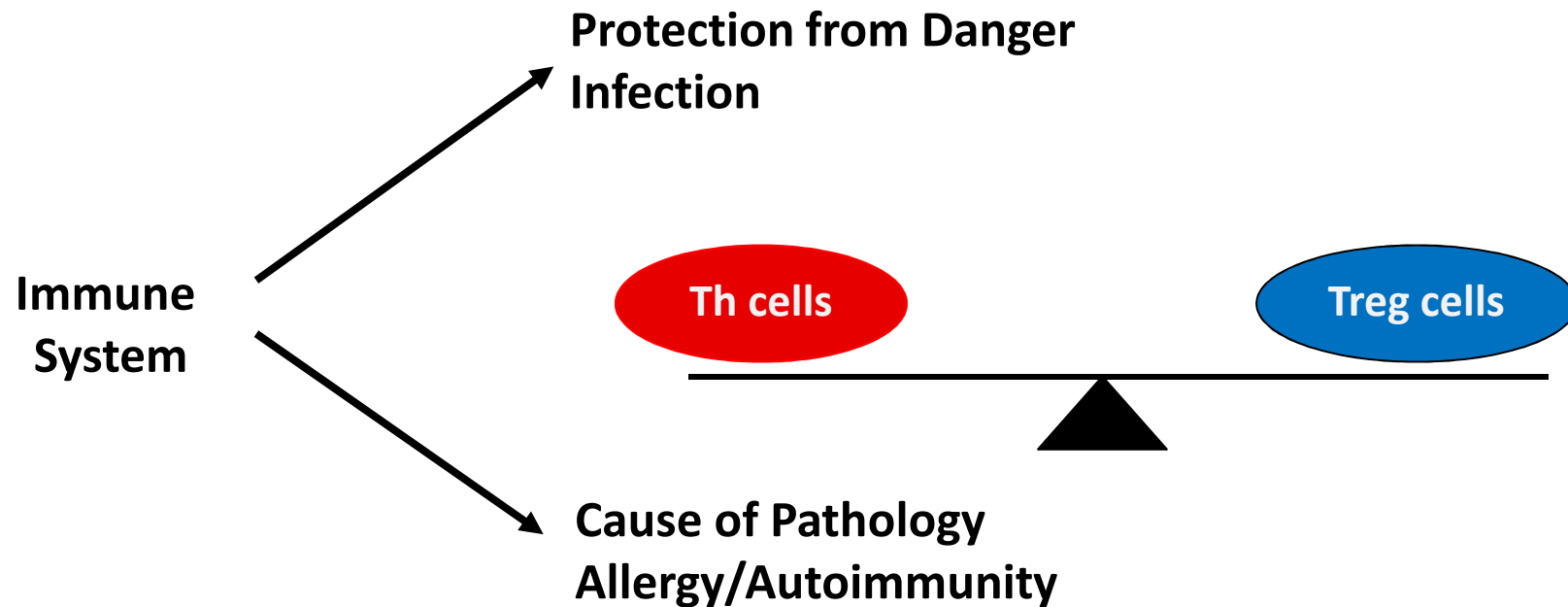
## The Problem

- Abnormal immune response can cause serious and life threatening conditions e.g. MS, Graves' disease, SLE, RA, transplant rejection, allergy, protein drug inactivation (e.g. Factor VIII)
- Current therapies treat symptoms or suppress immune system with potential to
  - Increase infections
  - Increase risk of cancer

## The Solution

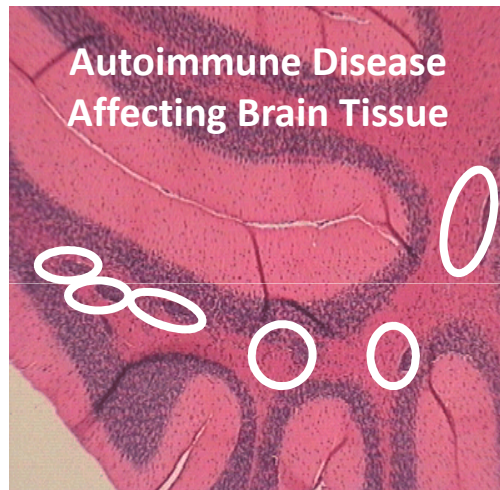
- Ideal therapeutic regime would re-instate normal immune balance and avoid global immune suppression
- The Apitope approach to allergy and autoimmune disorders treatment using therapeutic peptides with good evidence of efficacy

# The Immune System

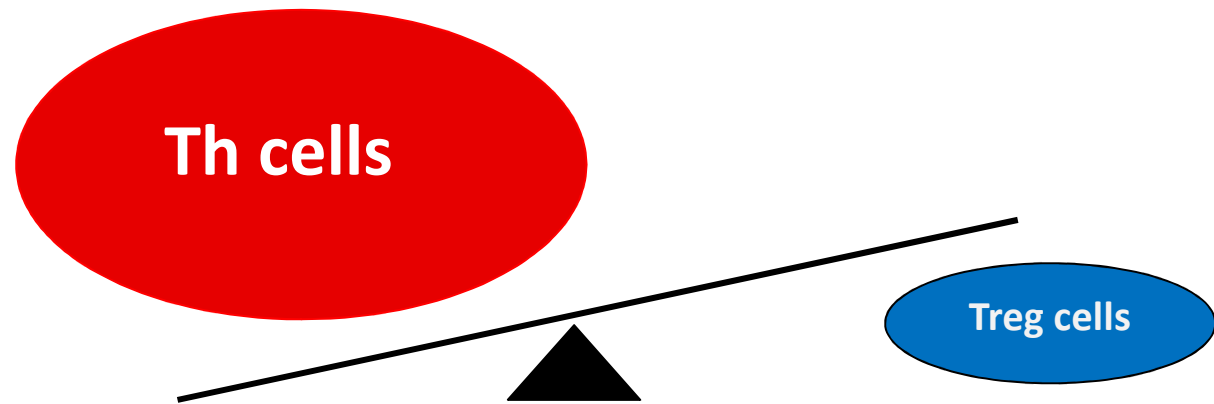


Hypersensitivity diseases are caused by the immune system responding excessively strongly to a self antigen (autoimmunity) or a foreign antigen (allergy)

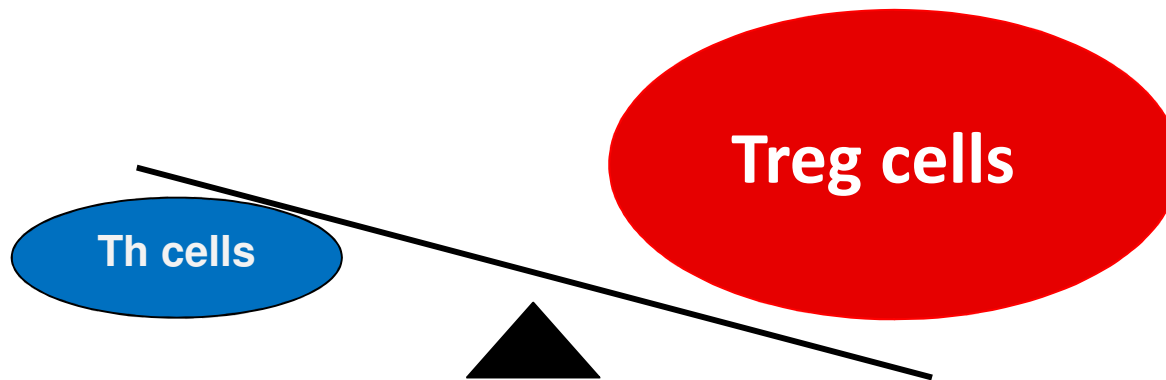
# Abnormal Response to Antigen Leads to Imbalance of Immune System and to Tissue Damage



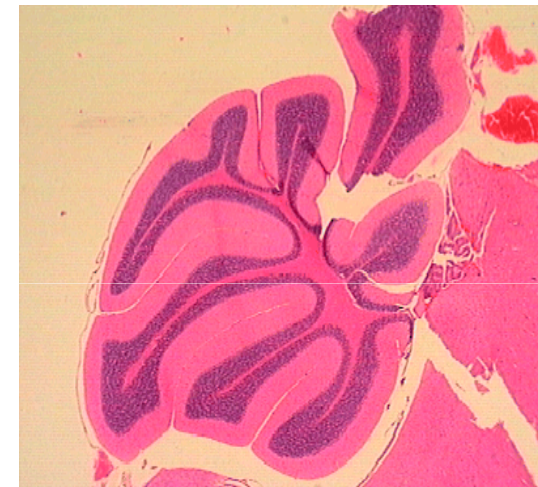
Cells capable of causing tissue damage



# Apitope™ Treatment Increases Treg to Restore Immune Balance and Protects Tissues From damage

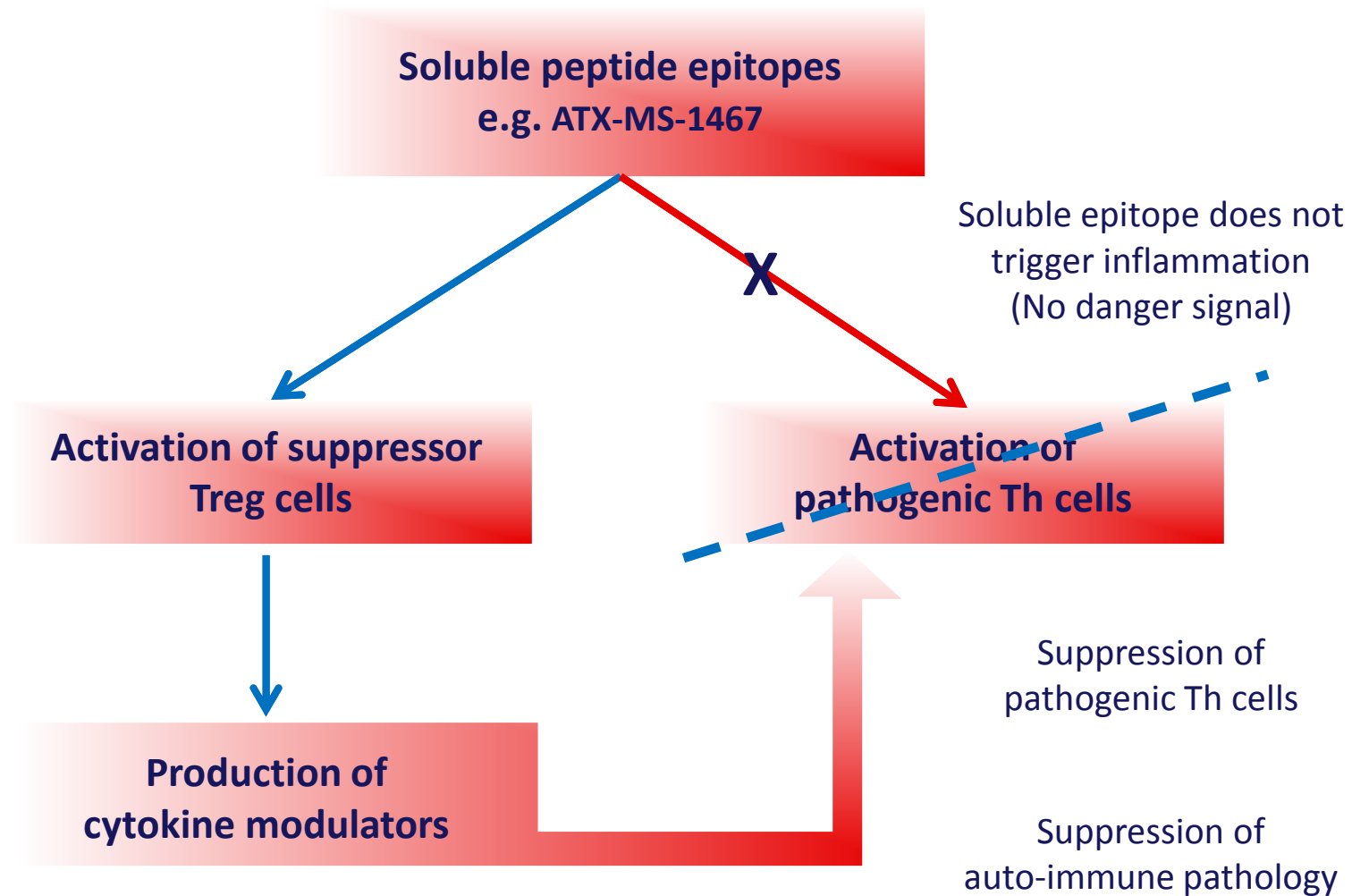


**Brain Tissue Protected  
By Regulatory T Cells**



**Natural Regulatory  
(CD25, FoxP3)  
And Induced Suppressor  
Cells**

# Apitope™ Mechanism of Action Initiates a Natural Immune System Regulatory Process



# Peptides Therapy: a well Established Approach for Prevention and Treatment of Disease in Animal Models

Disease	Species	Peptide	Dose/animal & route	Effective	Reference
MS	Mouse	MBP Ac1-9	100 mg i.n.	✓	Metzler et al 1993
MS	Mouse	MBP Ac1-9	100 mg i.p.	✓	Liu et al 1995
MS	Mouse	PLP 139-151	100 mg i.n.	✓	Anderton et al 1998
MS	Rat	MBP 87-99	5 x 120 mg i.n	✓	Liu, et al 1998
Arthritis	Mouse	Collagen II 245-270	3 x 100 mg i.n.	✓	Chu et al 1999
Arthritis	Rat	HSP60 176-190	3 x 100 mg i.n. or s.c.	✓	Prakken et al 1997
Diabetes	Mouse	4 GAD peptides	200 mg i.n.	✓	Tian et al 1996
Diabetes	Mouse	Insulin 9-23	100 mg i.n. or s.c.	✓	Daniel et al 1996
Diabetes	Mouse	HSP60 p277	50 mg i.p.	✓	Elias et al 1991
Myasthenia	Mouse	3 AChR peptides	50 mg i.n.	✓	Karachunski et al 1997
Neuritis	Rat	P0 180-199	10 x 6 mg i.n.	✓	Zou et al 1999

# Peptide Therapies are Effective in Human Clinical Trials

Disease	Peptide	Efficacy	Treg	Reference
Bee Venom Allergy	PLA2	✓	✓	Muller et al,1998
Cat Dander Allergy	Fel d 1	✓	✓	Oldfield et al, 2002
Rheumatoid Arthritis	Bacterial hsp dnaJP1	✓	✓	Prakken et al, 2002 Prakken et al, 2004
Multiple Sclerosis	Copaxone	✓	✓	Duda et al, 2000 Putheti et al, 2003
Multiple Sclerosis	ATX-MS-1467	[✓]	✓	Apitope, 2008
Type I Diabetes	Hsp 60 p277	✓	✓	Zanin-Zhorov et al, 2006

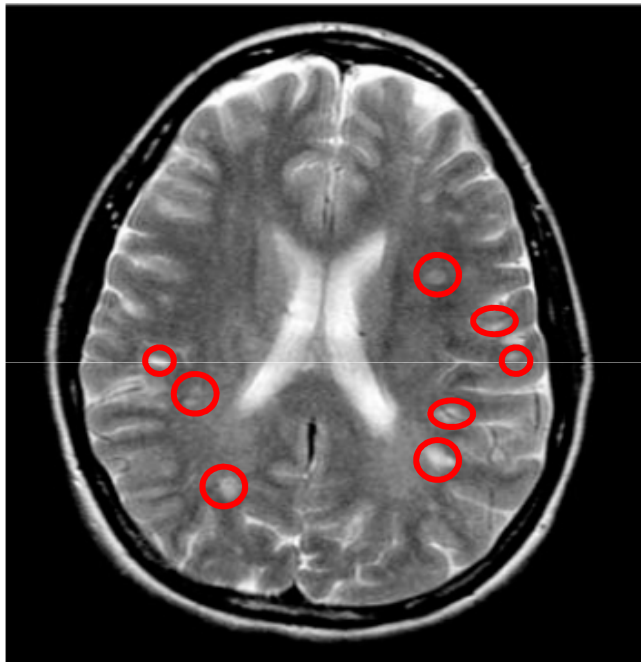
# The Apitope Approach

- Mechanism of Action has proven efficacy in experimental models
  - Species
  - Diseases
- Repeated treatment required
- Safe and well tolerated
- Apitope platform enables design and selection of effective peptides

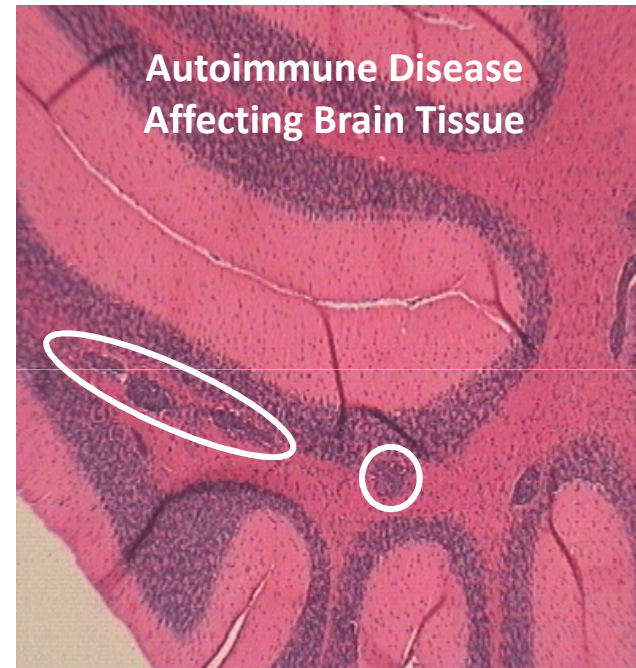
# Multiple Sclerosis: ATX-MS-1467

- Synthetic **soluble** copies of **peptide** fragments of human MBP
- *In silico* analysis shows ATX-MS-1467 recognised by >92% of population
- **High specificity**
  - < 0.000 06 % of CD4<sup>+</sup> Tcells will respond to ATX-MS-1467
    - No widespread stimulation of T cells will occur
    - Immune response to infection unaffected
- **Efficacy** in MS models and immune system both *in vivo* and *in vitro*
- **Safe and well tolerated** in preclinical safety and toxicity tests
- MHRA approved first in man Phase I clinical trial in SPMS patients completed
  - No treatment related SAE reported
  - Preliminary evidence of efficacy

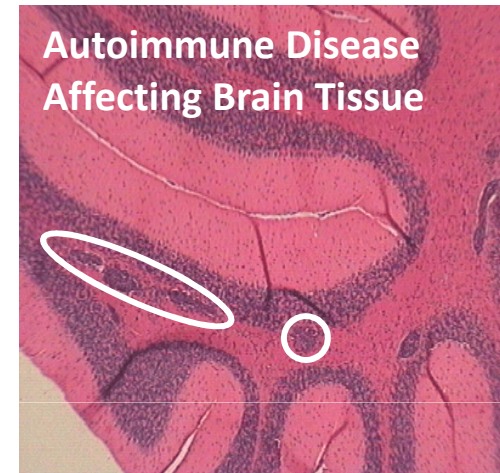
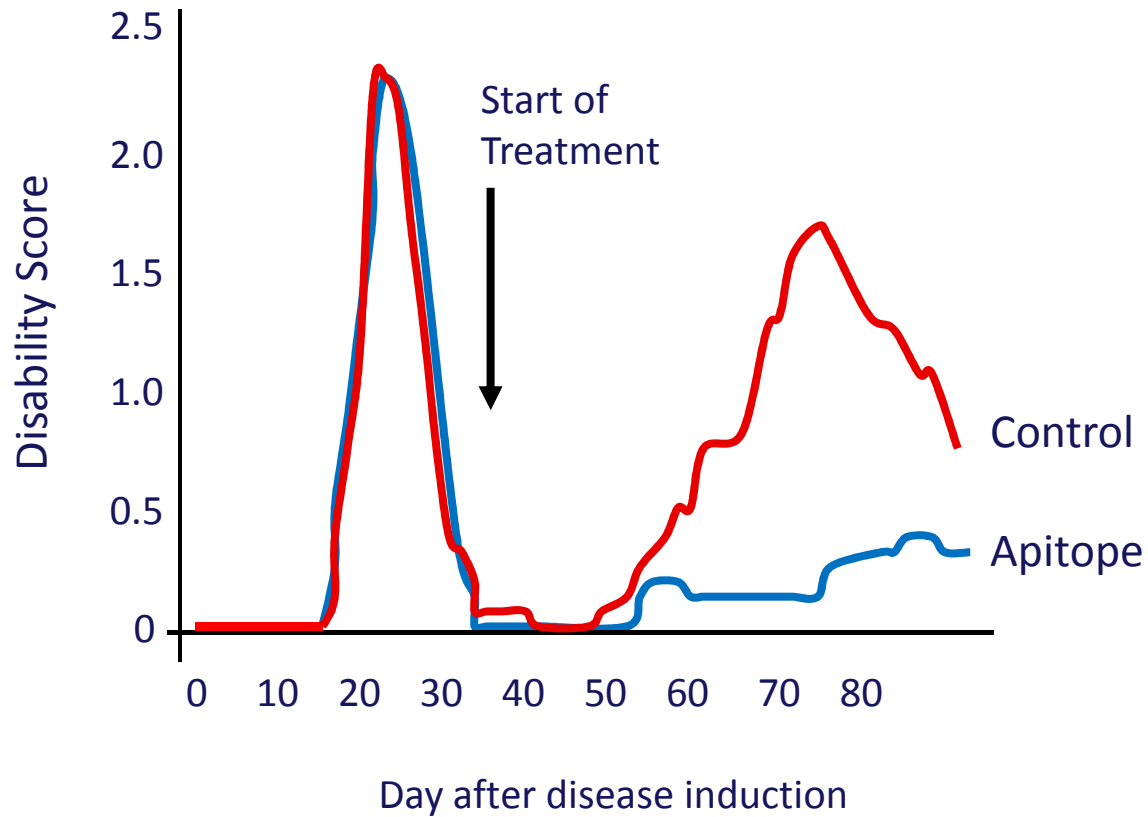
# Clinical and Pre-clinical Models have Similar Characteristics



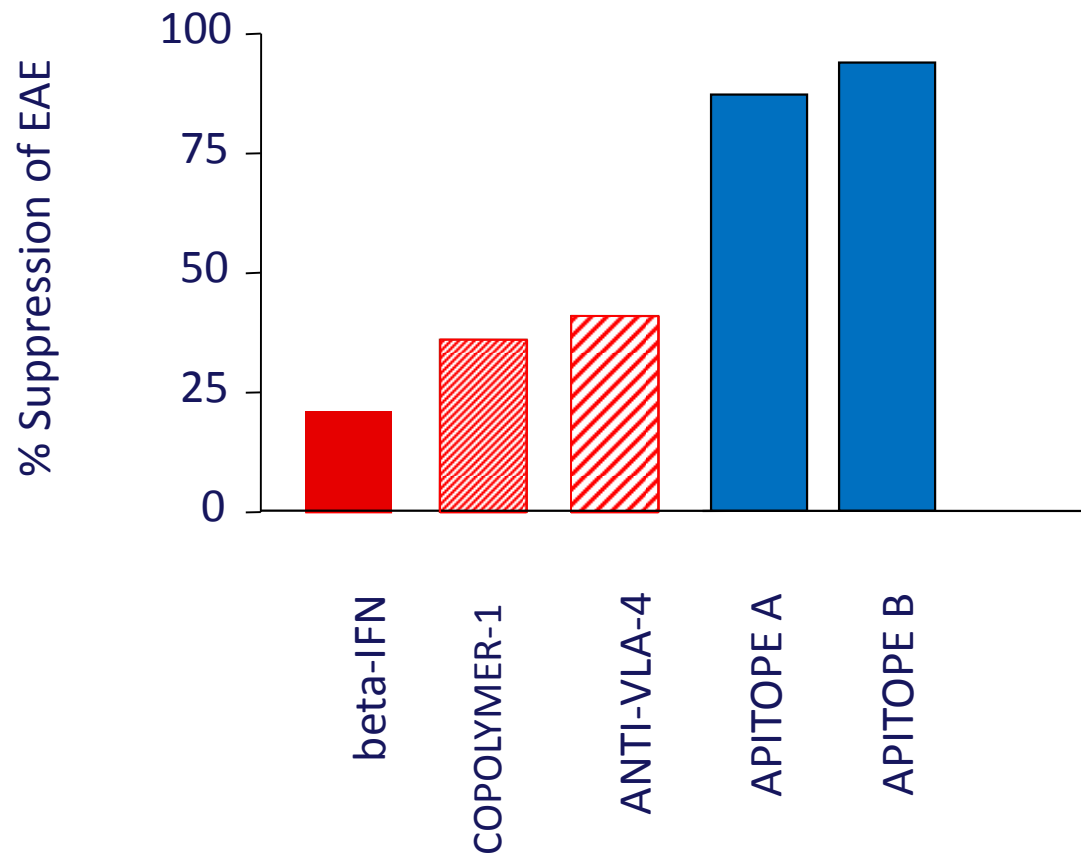
**MRI brain scan from newly diagnosed 33 year-old woman**



# Modified Disease Progression in Pre-clinical Model of RRMS



# Apitopes™: Improved Efficacy in Pre-clinical EAE Model Compared With Leading Products



# The Apitope Platform Identifies Peptide Product Candidates Rapidly From Antigenic Protein

Bioinformatic prediction of T cell epitopes



Screen peptide epitopes against antigen specific bank of T cell hybridomas from HLA transgenic mice



Select peptides giving positive responses

**Potential Apitopes**



Design apitopes™ and test in HLA transgenic mice models *in vivo*  
Test apitope™ responses in patient PBMC

# ATX-MS-1467: T Cell Epitopes of Myelin Basic Protein



**Apitopes**

**MS 1**  
**30-44**  
**DQ 6**

**MS 7**  
**83-99**  
**DR 15**

**MS 4**  
**131-145**  
**DQ 6**

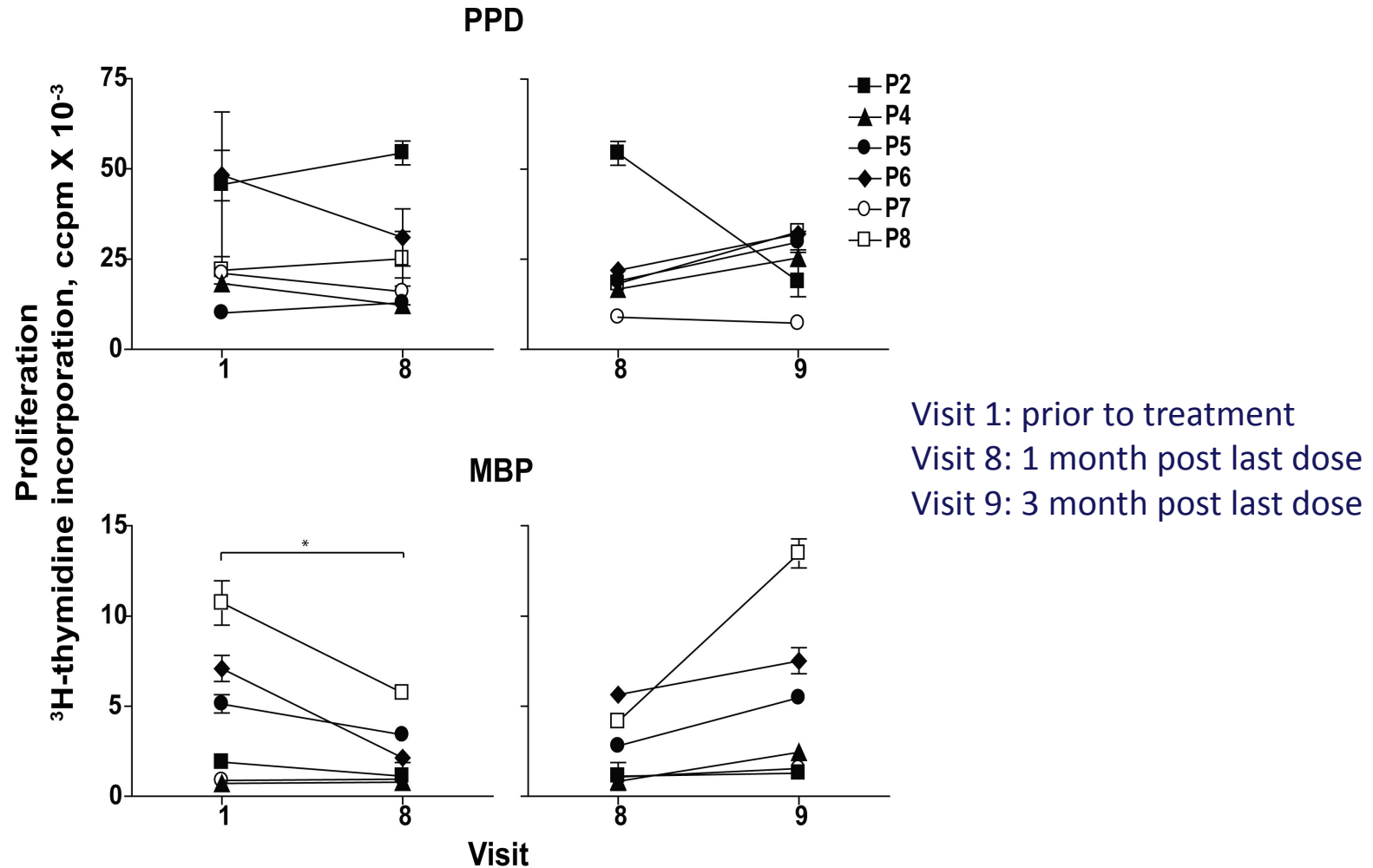
**MS 6**  
**140-154**  
**DR 15**

*In silico* analysis shows that ATX-MS-1467 will be recognised by >92% of population

# ATX-MS-1467 Trial 001: Safe and Well Tolerated

Parameter	Result
Blood Tests	No clinically significant changes
Vital Signs	No abnormalities observed
ECG	No clinically significant abnormalities
Injection site reactions	Two mild, transient, localised reactions reported
MRI Scans	No deterioration from baseline
Physical Exam	Unchanged from baseline

# Immune Responses Before and After ATX-MS-1467 Treatment in SPMS Patients



Repeated treatment with ATX-MS-1467 required to maintain suppression

# Solid IP Base

- Peptide Selection Method and Tolerogenic Peptides from MBP
  - Publication date 28th February 2002
  - Method for selecting epitopes that induce tolerance and CoM
- Tolerogenic Peptides from MBP
  - Filed January 2003 with a priority date of 01/02/2002
- ATX-MS-1467 treatment of MS and optic neuritis
  - Filed October 2007
- Tolerogenic Peptides from Factor VIII
  - Filed December 2008
- Modified Peptides from Factor VIII
  - Filed May 2009
- Disease Markers MS
  - Filed April 2007
- Disease Biomarkers MS
  - Filed April 2007

# Apitope

- Experienced management team
- High Speed apitope™ therapeutic peptide discovery platform
- Applicable across broad range of diseases
- Addressing significant potential markets
- Innovative pipeline
- Major pharma endorsement
- Positioned for substantial shareholder return

Partner of choice for pharmaceutical companies keen to develop disease modifiers for autoimmune conditions