

Q1 2018



**Developing medicines based on cannabinoid science**

Jim DeMesa, MD, MBA  
*Chief Executive Officer*





# Important Notice

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## Cautionary Note Regarding Forward-Looking Statements

TO THE EXTENT STATEMENTS CONTAINED IN THE FOLLOWING PRESENTATION ARE NOT DESCRIPTIONS OF HISTORICAL FACTS REGARDING THE COMPANY, THEY SHOULD BE CONSIDERED “FORWARD-LOOKING STATEMENTS,” AS DESCRIBED IN THE PRIVATE SECURITIES LITIGATION REFORM ACT OF 1995, THAT REFLECT MANAGEMENT’S CURRENT BELIEFS AND EXPECTATIONS. YOU CAN IDENTIFY FORWARD-LOOKING STATEMENTS BY WORDS SUCH AS “ANTICIPATE,” “BELIEVE,” “COULD,” “ESTIMATE,” “EXPECT,” “FORECAST,” “GOAL,” “HOPE,” “HYPOTHESIS,” “INTEND,” “MAY,” “PLAN,” “POTENTIAL,” “PREDICT,” “PROJECT,” “SHOULD,” “STRATEGY,” “WILL,” “WOULD,” OR THE NEGATIVE OF THOSE TERMS, AND SIMILAR EXPRESSIONS THAT CONVEY UNCERTAINTY OF FUTURE EVENTS OR OUTCOMES. FORWARD-LOOKING STATEMENTS CONTAINED IN THESE PRESENTATIONS INCLUDE, BUT ARE NOT LIMITED TO, STATEMENTS REGARDING: (I) THE SUCCESS AND TIMING OF OUR PRODUCT DEVELOPMENT ACTIVITIES AND CLINICAL TRIALS; (II) OUR ABILITY TO DEVELOP OUR PRODUCT CANDIDATES; (III) OUR PLANS TO RESEARCH, DISCOVER, EVALUATE AND DEVELOP ADDITIONAL POTENTIAL PRODUCT, TECHNOLOGY AND BUSINESS CANDIDATES AND OPPORTUNITIES; (IV) OUR ABILITY TO DEVELOP AND MANUFACTURE OUR PRODUCT CANDIDATES AND TO IMPROVE THE MANUFACTURING PROCESS; (V) OUR ABILITY TO ATTRACT AND RETAIN KEY SCIENTIFIC OR MANAGEMENT PERSONNEL; (VI) THE ANTICIPATED TIMING OF CLINICAL DATA AVAILABILITY; (VII) OUR ABILITY TO MEET OUR MILESTONES; (VIII) OUR EXPECTATIONS REGARDING OUR ABILITY TO OBTAIN AND MAINTAIN INTELLECTUAL PROPERTY PROTECTION; AND (IX) THE IMPACT OF CAPITAL MARKET CONDITIONS ON US. FORWARD-LOOKING STATEMENTS ARE SUBJECT TO KNOWN AND UNKNOWN FACTORS, RISKS AND UNCERTAINTIES THAT MAY CAUSE ACTUAL RESULTS TO DIFFER MATERIALLY FROM THOSE EXPRESSED OR IMPLIED BY SUCH FORWARD LOOKING STATEMENTS. UNDUE RELIANCE SHOULD NOT BE PLACED ON FORWARD-LOOKING STATEMENTS. WE UNDERTAKE NO OBLIGATION TO PUBLICLY UPDATE ANY FORWARD-LOOKING STATEMENTS. THE COMPANY’S INVESTIGATIONAL DRUG PRODUCTS HAVE NOT BEEN APPROVED OR CLEARED BY THE FDA.



## Emerald Health Pharmaceuticals

Focused on developing patented synthetic cannabinoid-derived drug candidates to treat diseases with unmet medical need

Established: 2017

Headquarters: San Diego, CA, USA

Status: Private





# Key Highlights

15 years of cannabinoid science, broad patent coverage, foundation is the endocannabinoid system (ECS)

**Synthetic cannabinoid-derivative pharmaceutical drug developer**

**Multiple patented CBD & CBG derivatives for treating a range of disorders with unmet needs**

**Phase I human study planned for 2018**

**Orphan Drug status granted by FDA and EMA for scleroderma and by FDA for Huntington's disease**

**Experienced management in pharma/biotech**



# Why Cannabinoid-Derived Drugs?

## NATURAL

The endocannabinoid system (ECS) is an internal system in our bodies that has been shown to foster overall health with two primary receptors:

**CB1** and **CB2**

## THERAPEUTIC

Positive effects through influence on the ECS

## SAFE

**Cannabidiol (CBD)** & **cannabigerol (CBG)** are non-psychootropic, with low toxicity

## Endocannabinoid System

These receptors are part of the endocannabinoid system which impact physiological processes affecting pain modulation, memory, and appetite plus anti-inflammatory effects and other immune system responses. The endocannabinoid system comprises two types of receptors, CB1 and CB2.

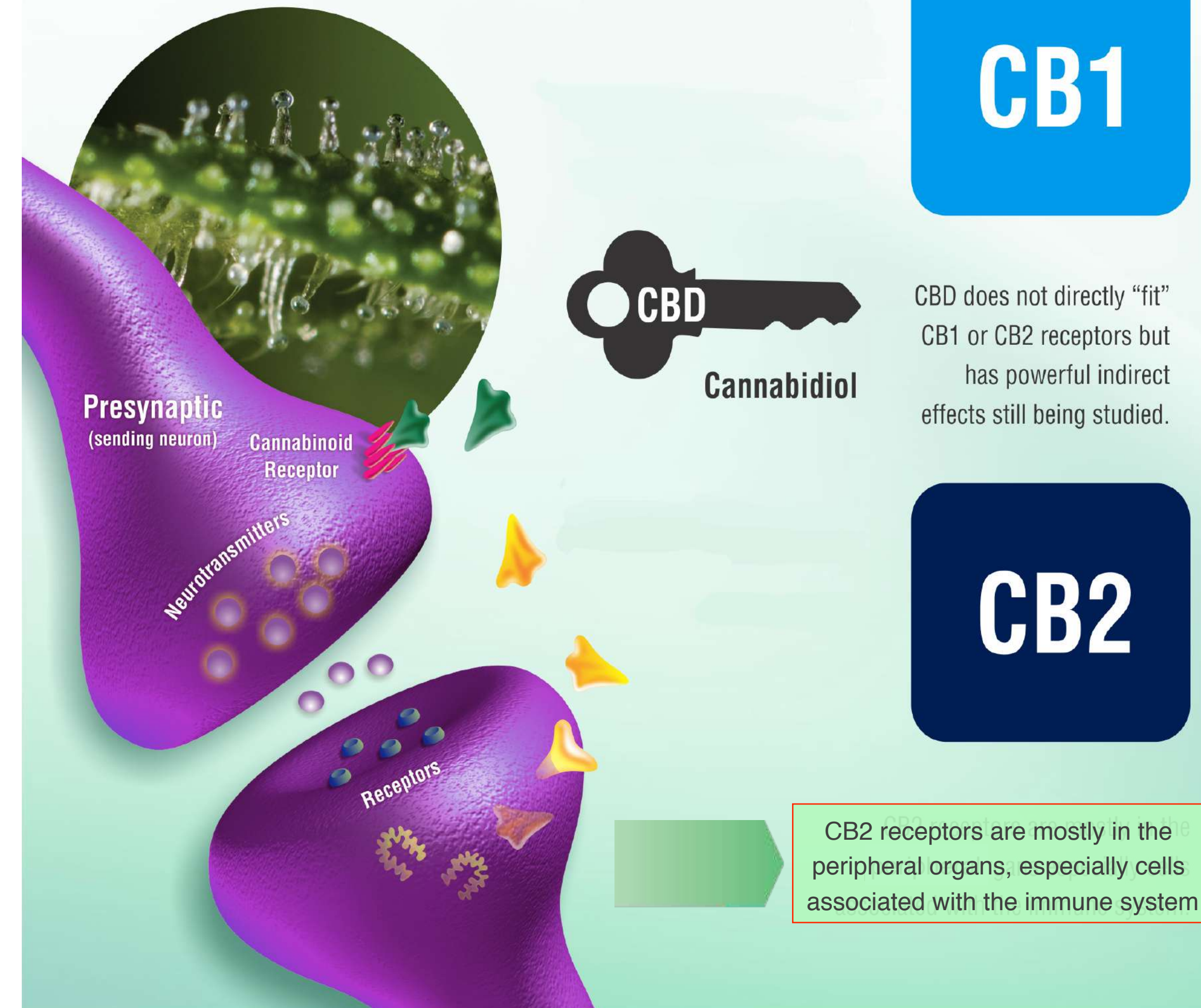
CB1 receptors are primarily found in the brain and central nervous system, and to a lesser extent in other tissues.

**CB1**

CBD does not directly “fit” CB1 or CB2 receptors but has powerful indirect effects still being studied.

**CB2**

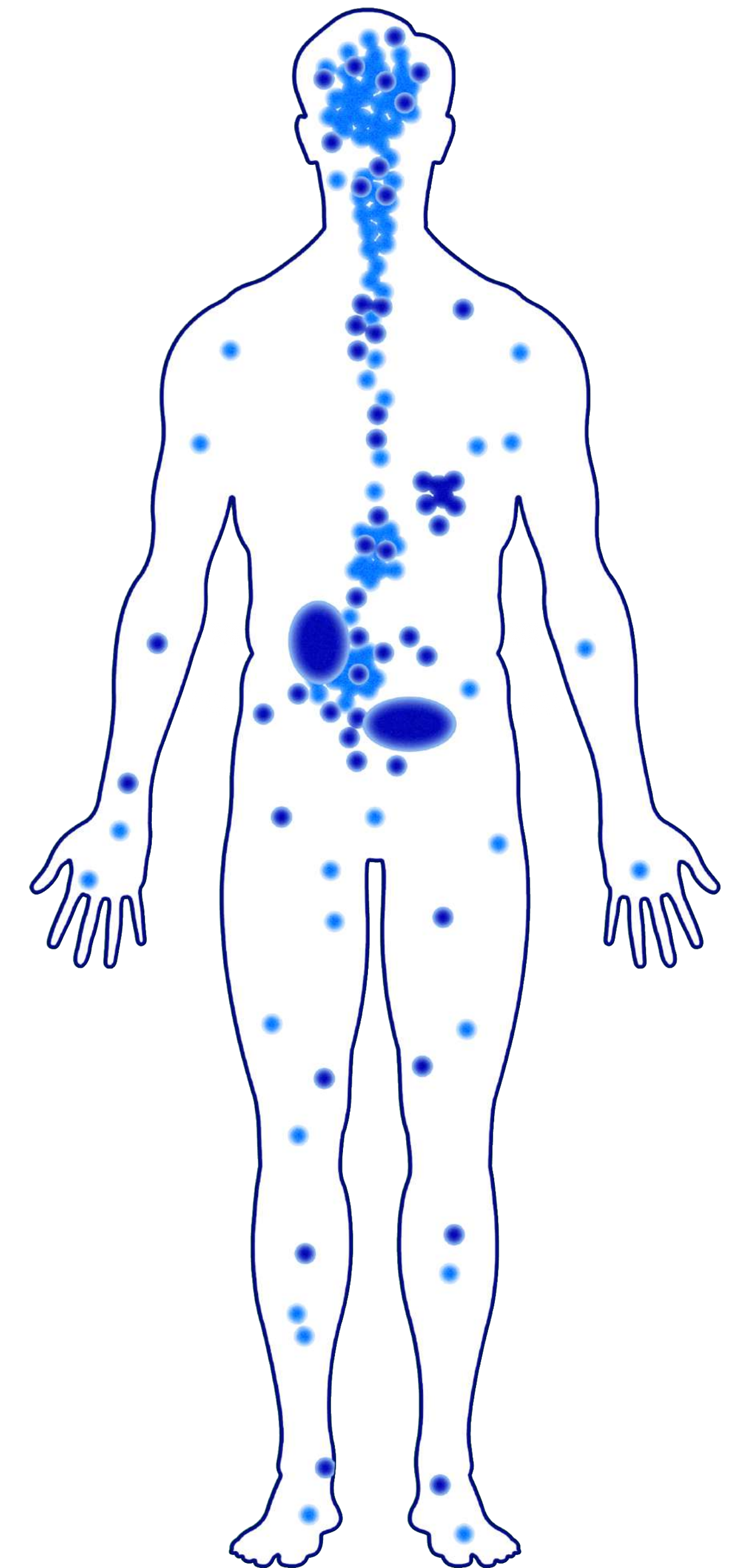
CB2 receptors are mostly in the peripheral organs, especially cells associated with the immune system





## Why Patented Synthetic Drugs?

- **IMPROVE** **CDB** & **CGB** receptor targeting
- **FOCUS** on receptors that can treat diseases with unmet medical need
- **DEVELOP** composition of matter patented cannabinoid new chemical entities (NCEs)
- **CREATE** a strong IP portfolio



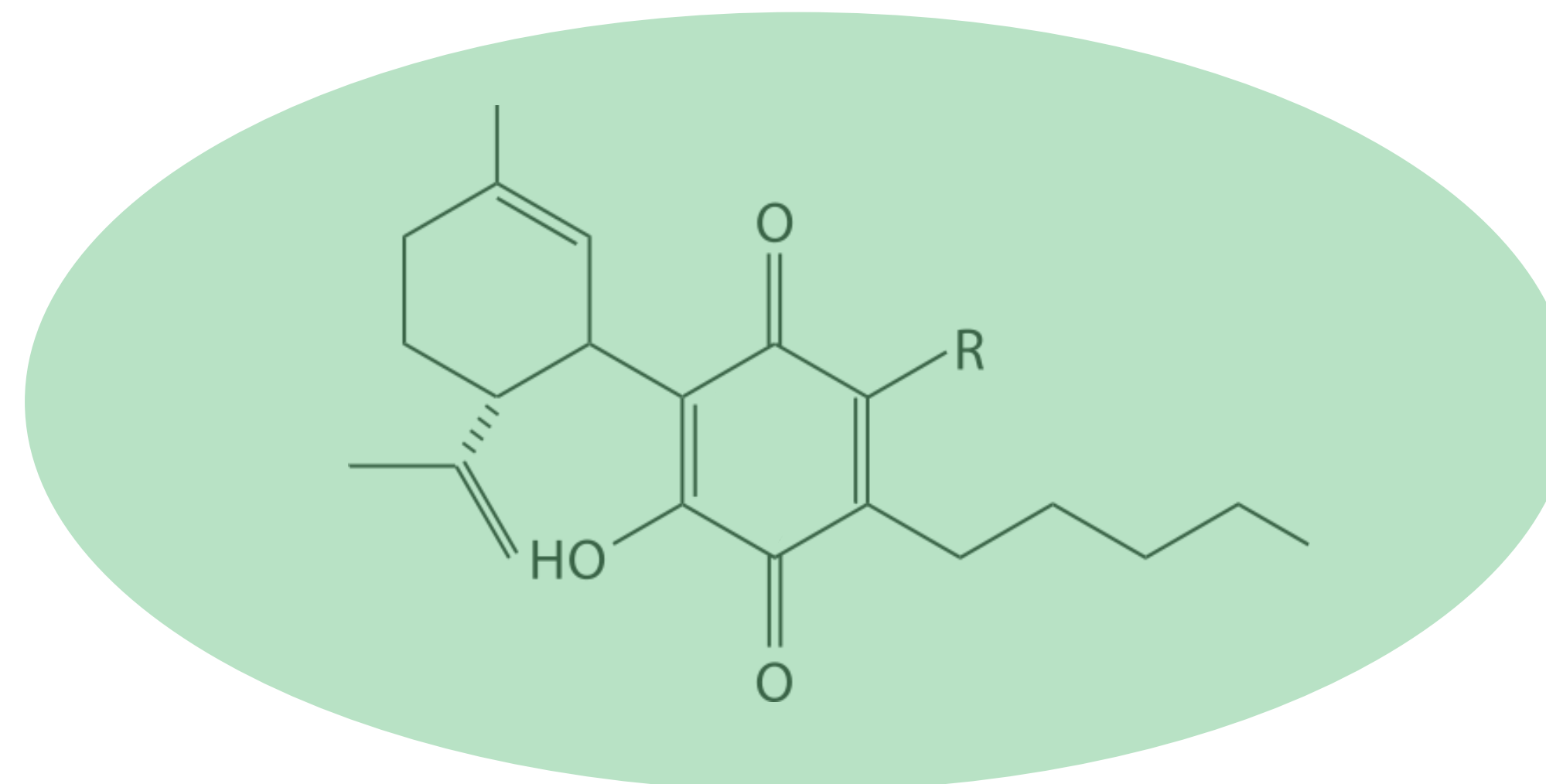


Patents: 6 Issued, 14 Pending

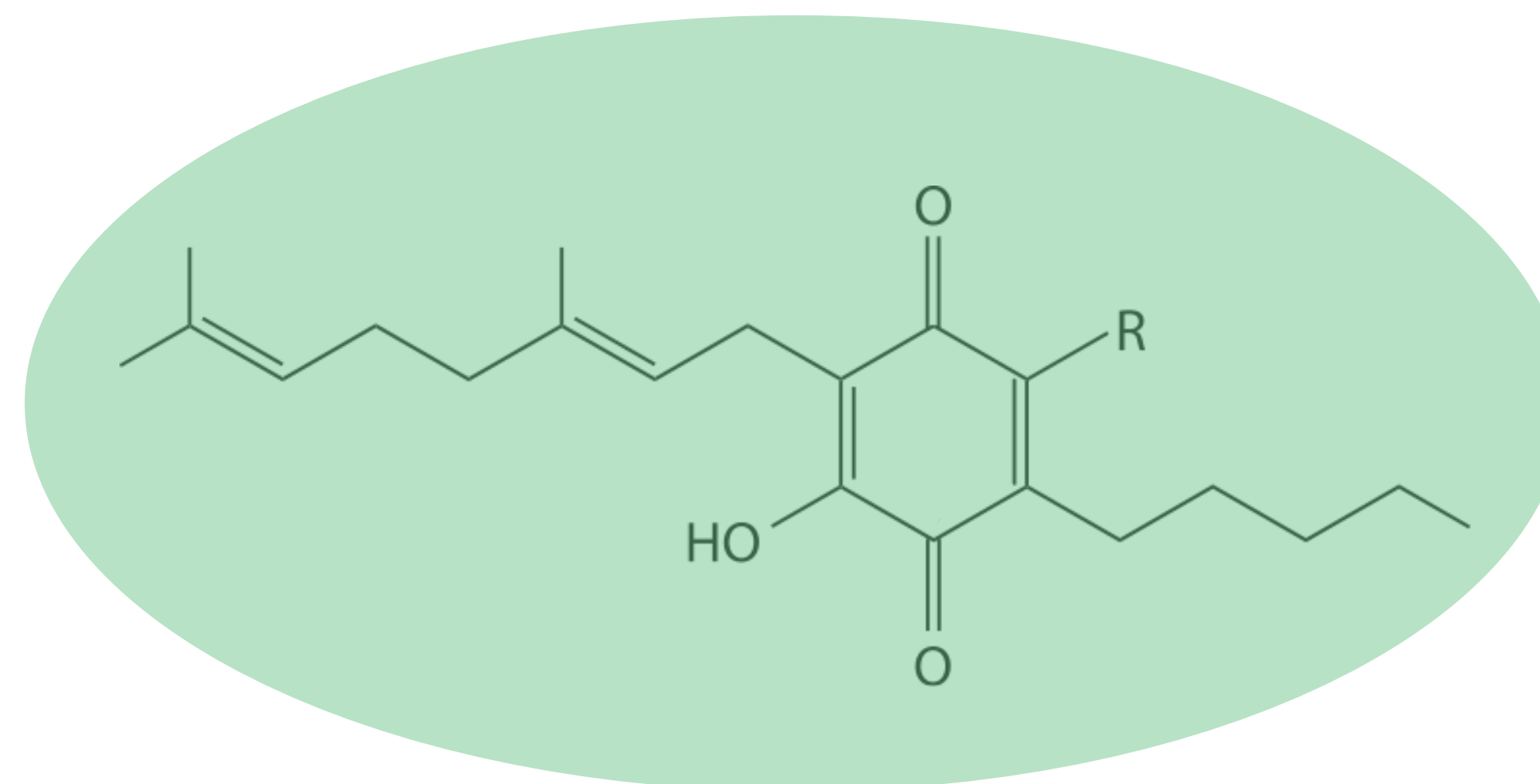
### Molecules in our NCE Library

- Composition of matter patents
- Protection to 2035
- Potential for multiple products and indications

14 patented **CBD** derivatives



11 patented **CBG** derivatives





## Significant Unmet Needs and Markets for 4 Initial Indications

### Multiple Sclerosis

900,000 patients in 7 major markets\*

### Scleroderma

Orphan Designation granted in the U.S. and E.U.

### Parkinson's Disease

10 million sufferers worldwide

### Huntingdon's Disease

Orphan Drug Designation granted in the U.S.

*\*Data per National Multiple Sclerosis Society and Global Data*





# Lead Product Candidates: Development Road Map

Proof-of-concept established for 4 initial indications

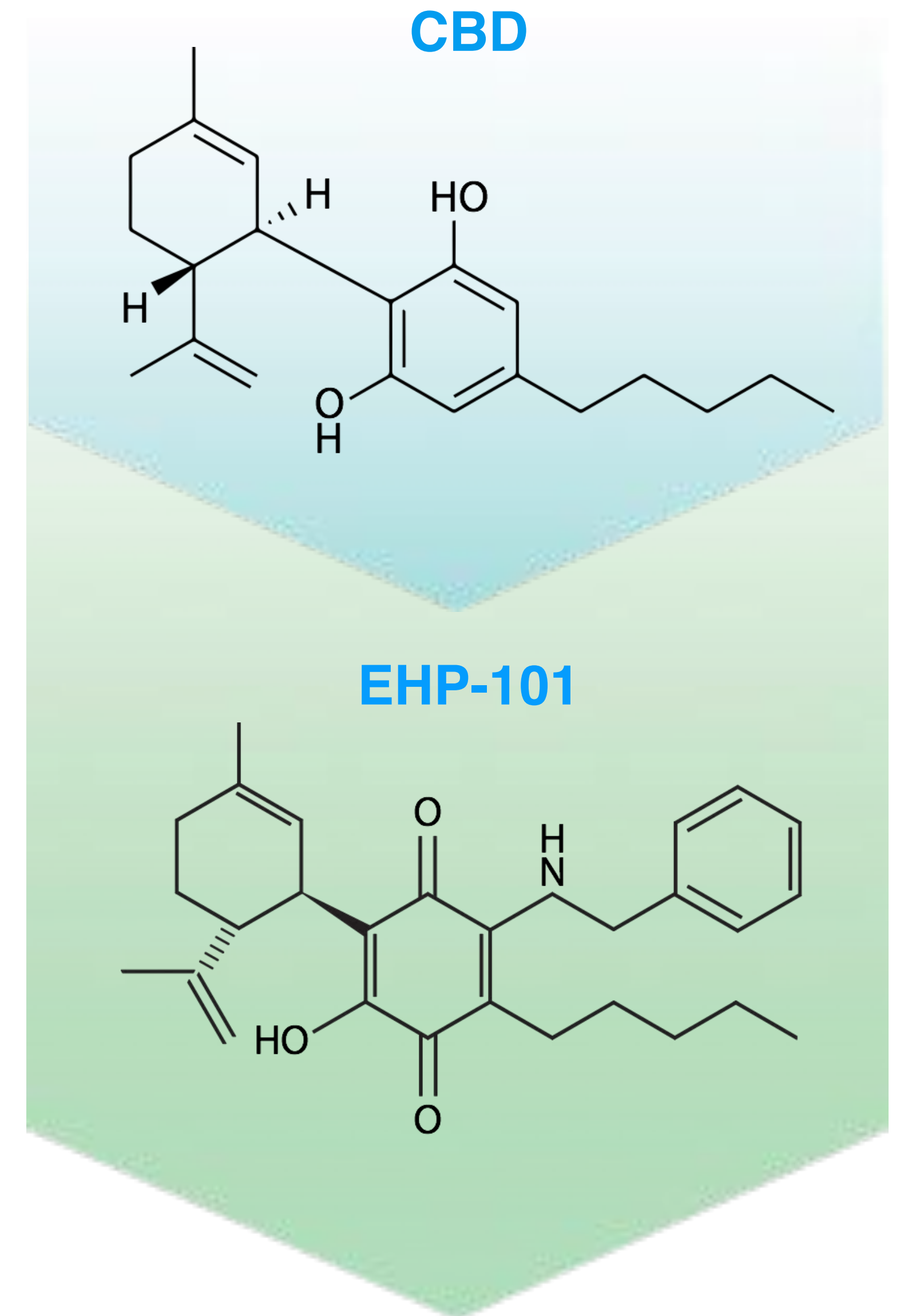


## Lead Product Candidate: EHP-101

### Cannabidiol (CBD) derivative

#### CBD:

- Does not bind to CB1
- Safe, anti-inflammatory, neuroprotective, analgesic, anti-proliferative
- Helps improve MS symptoms





# Why Multiple Sclerosis?

Chronic inflammatory, degenerative, demyelinating CNS disorder

- Our molecule targets the main receptors associated with MS
- Current medications are most effective only during the inflammatory phase; less potent as the disease transitions to a neurodegenerative process
- No effective disease-modifying drugs for progressive forms
- No therapies appear to re-myelinate damaged neurons

## Main symptoms of Multiple Sclerosis

### Central:

- Fatigue
- Cognitive impairment
- Depression
- Anxiety
- Unstable mood

### Visual:

- Nystagmus
- Optic neuritis
- Diplopia

### Speech:

- Dysarthria

### Throat:

- Dysphagia

### Musculoskeletal:

- Weakness
- Spasms
- Ataxia

### Sensation:

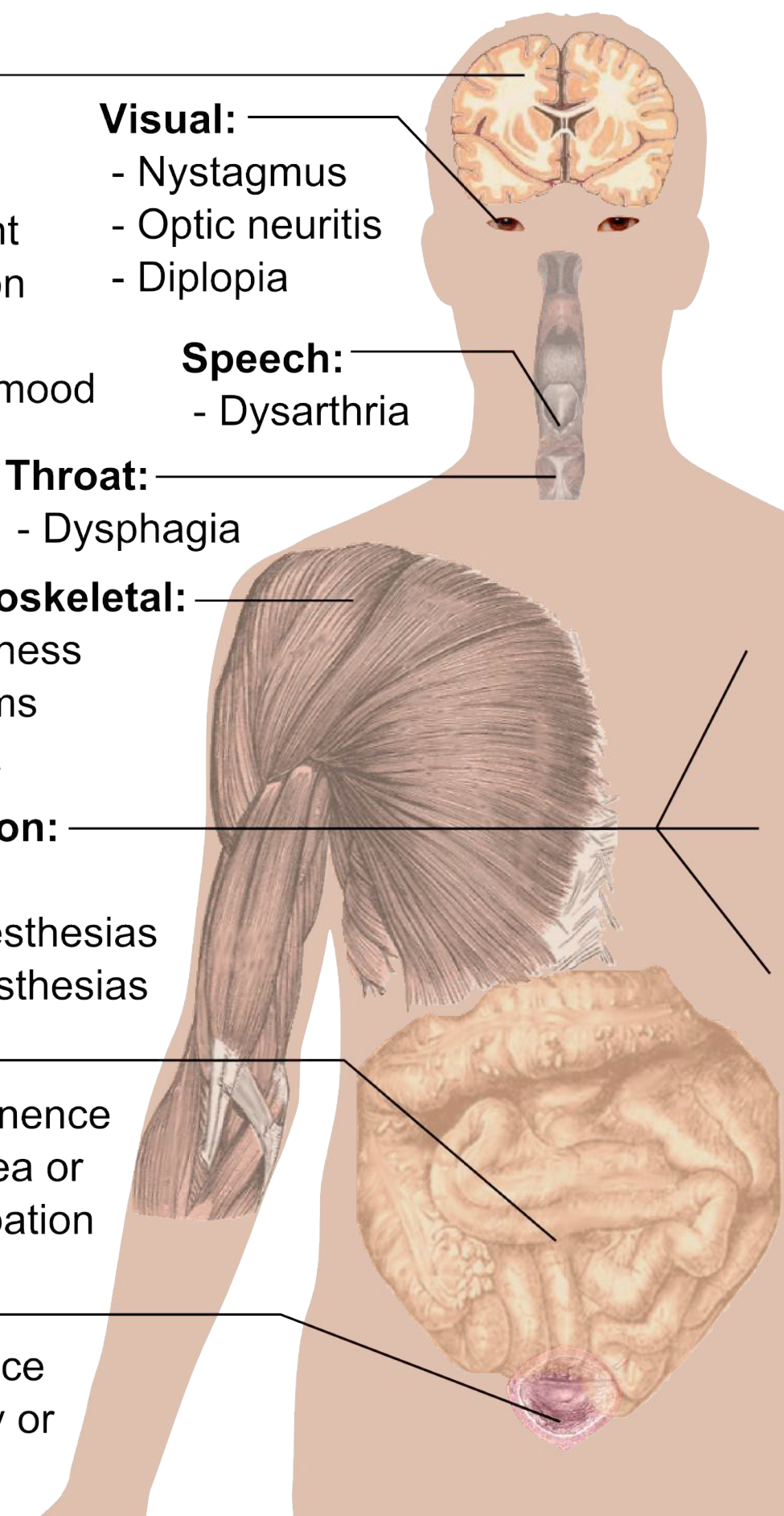
- Pain
- Hypoesthesias
- Paraesthesias

### Bowel:

- Incontinence
- Diarrhea or constipation

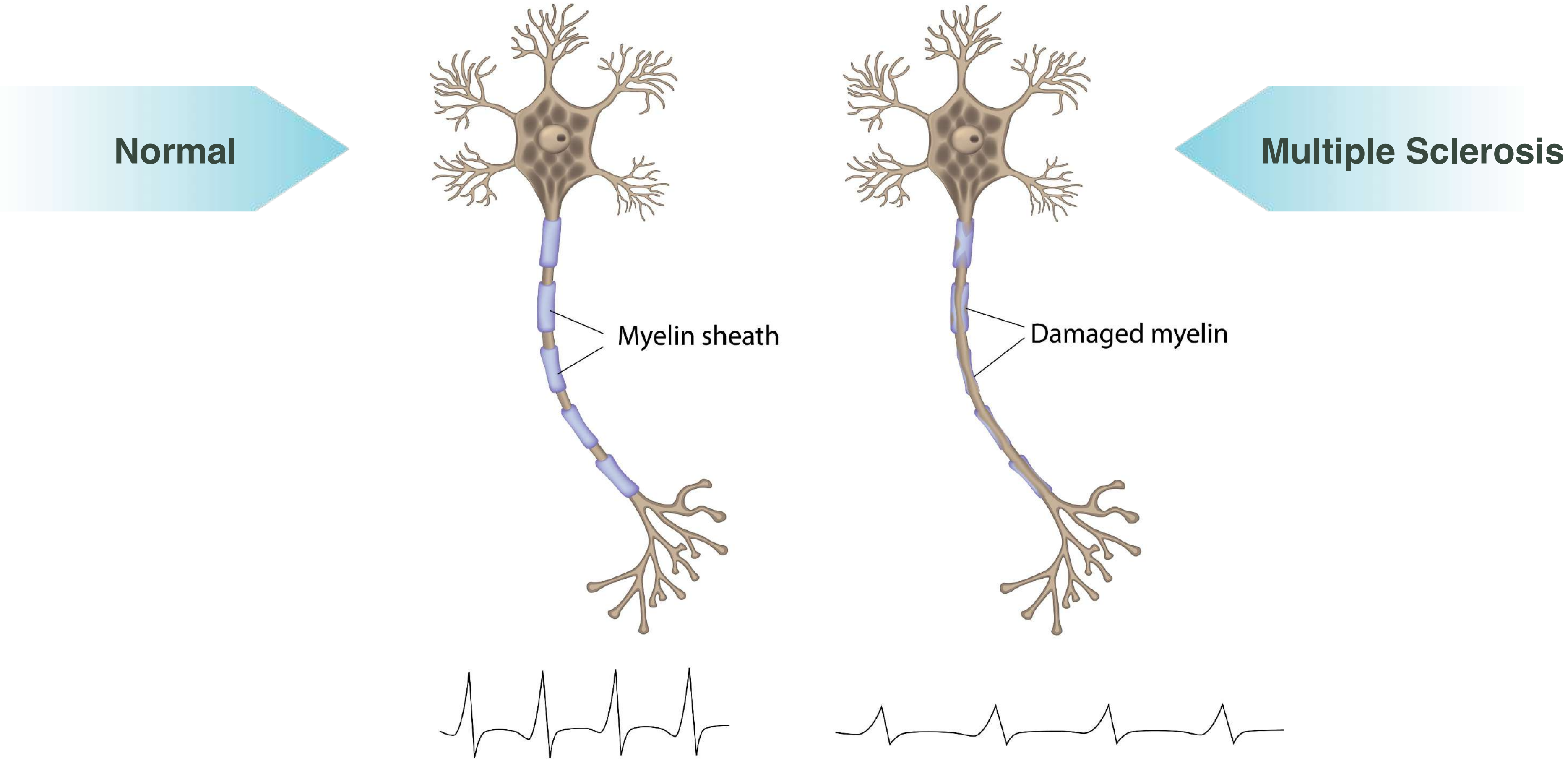
### Urinary:

- Incontinence
- Frequency or retention





# EHP-101 Can Potentially Re-Myelinate Nerves Damaged by MS







# EHP-101: Designed for Mechanism of Action

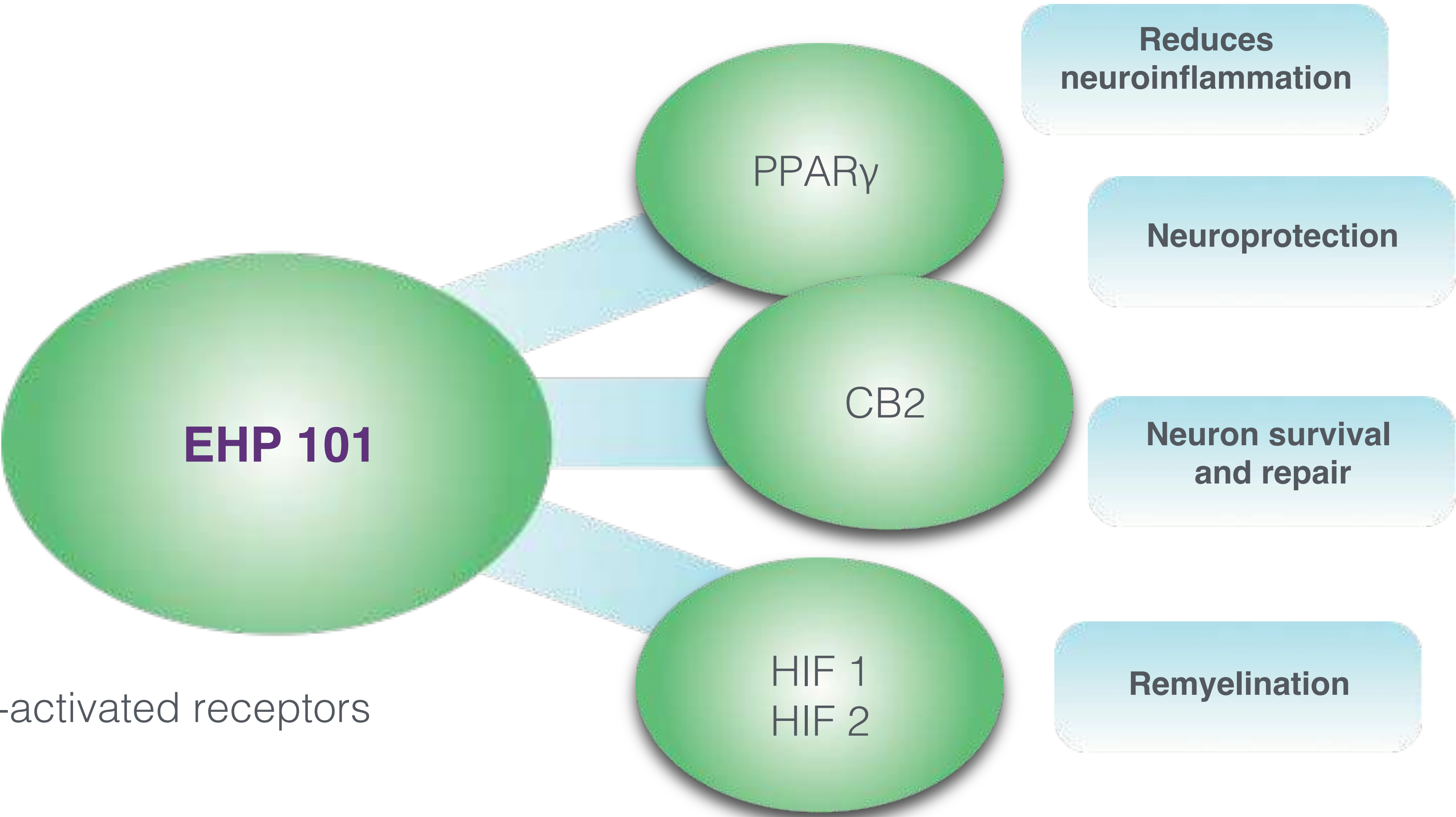
Our strategy:

To improve on CDB’s known positive effects by affecting validated targets in MS:

**PPAR $\gamma$ , CB2 and HIF**

PPAR: Peroxisome proliferator-activated receptors

HIF: Hypoxia inducible factor





## EHP-101 Multiple Sclerosis: Suggestive of Safety & Efficacy

- MoA consistent with validated MS targets
- Efficacy shown in relevant animal models of MS
- Effective at very low doses
- Low toxicity seen at much higher than therapeutic doses

**Human studies planned to start this year**

**Targets validated  
receptors related  
to MS**

**Oral treatment**

**Potentially  
disease-modifying**

**Broad IP protection**

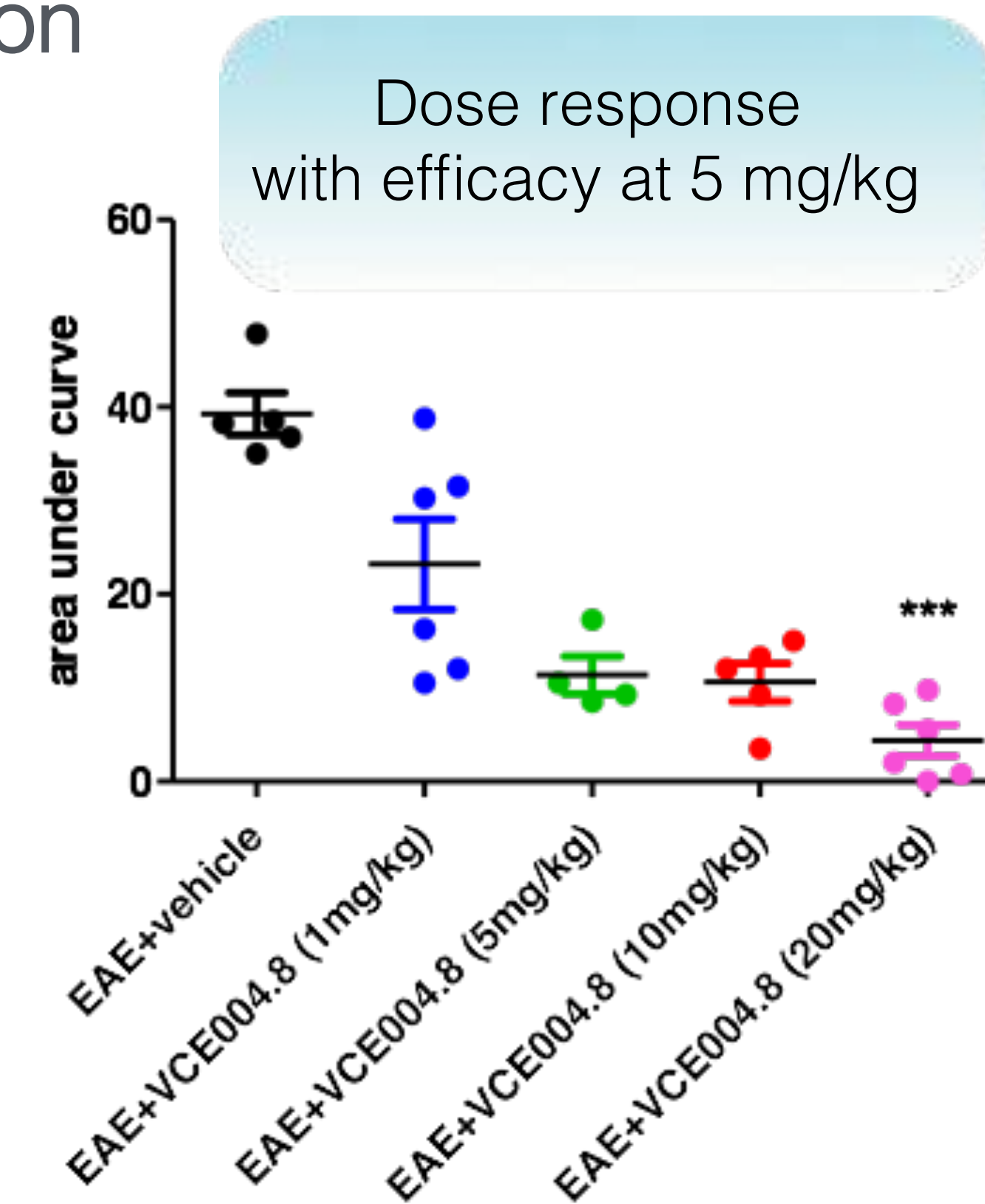
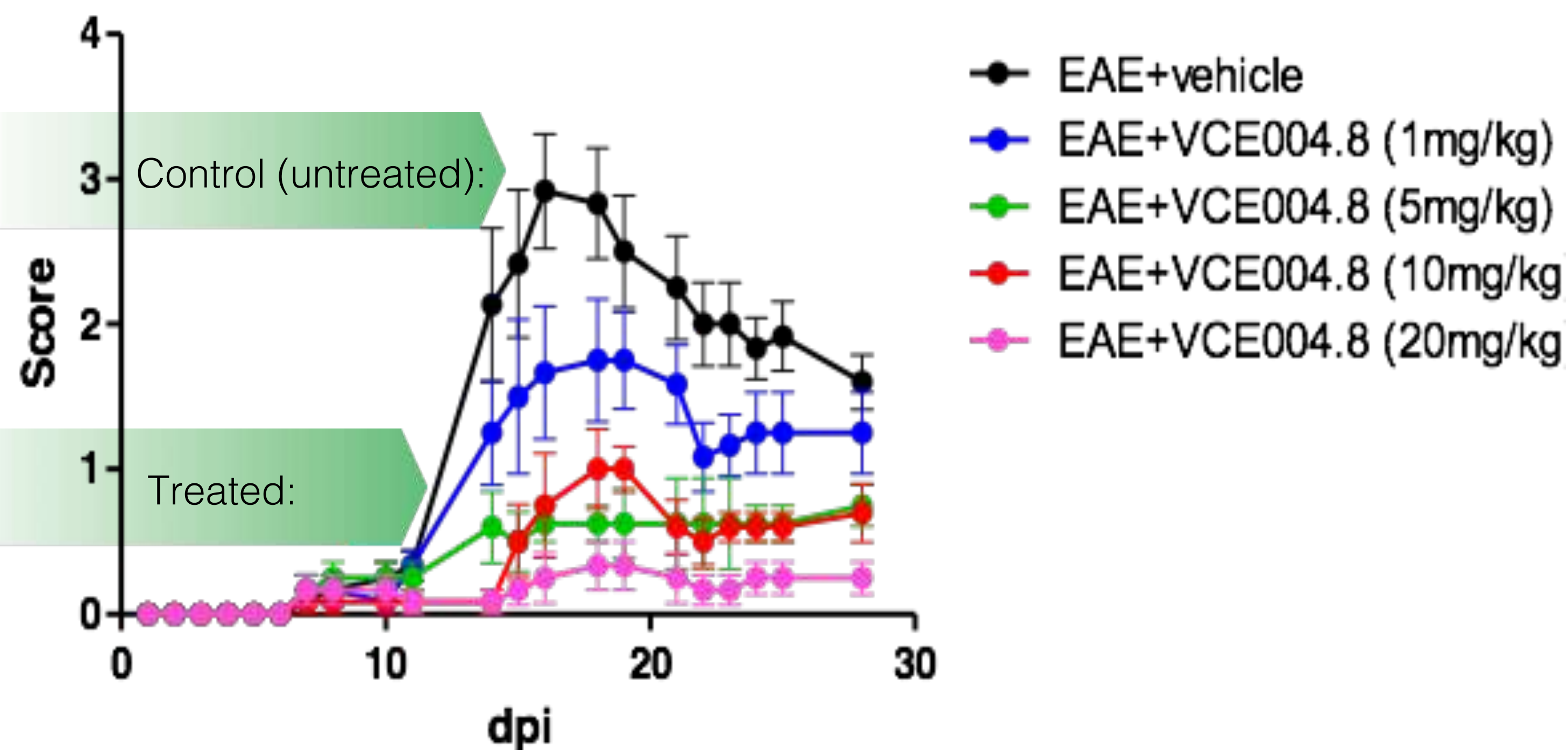
**Phase 1  
2018**



# EHP-101 Multiple Sclerosis: Efficacy Demonstrated

Two widely accepted animal models of MS (EAE & TMEV)

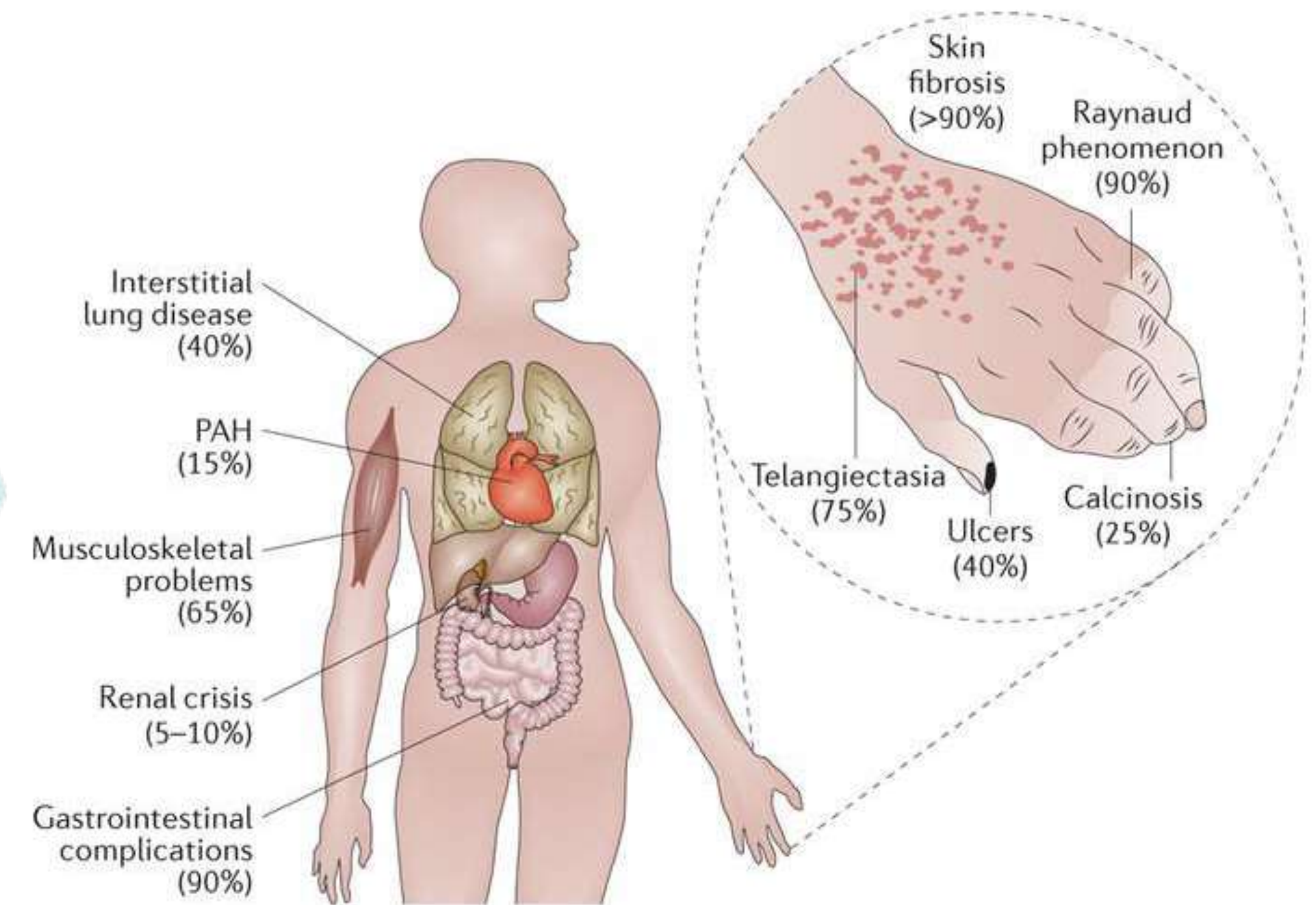
Significant reduction in clinical signs and disease progression



## EHP-101 Second Indication: Scleroderma (Systemic Sclerosis or SSc)

Chronic, systemic autoimmune disease causing fibrosis of skin and internal organs

- Rare, life-threatening disease
- No SSc-specific approved drugs
- Current therapies not effective and have significant toxicities
- Lung fibrosis is a common cause of death (~60% mortality in 10 years)



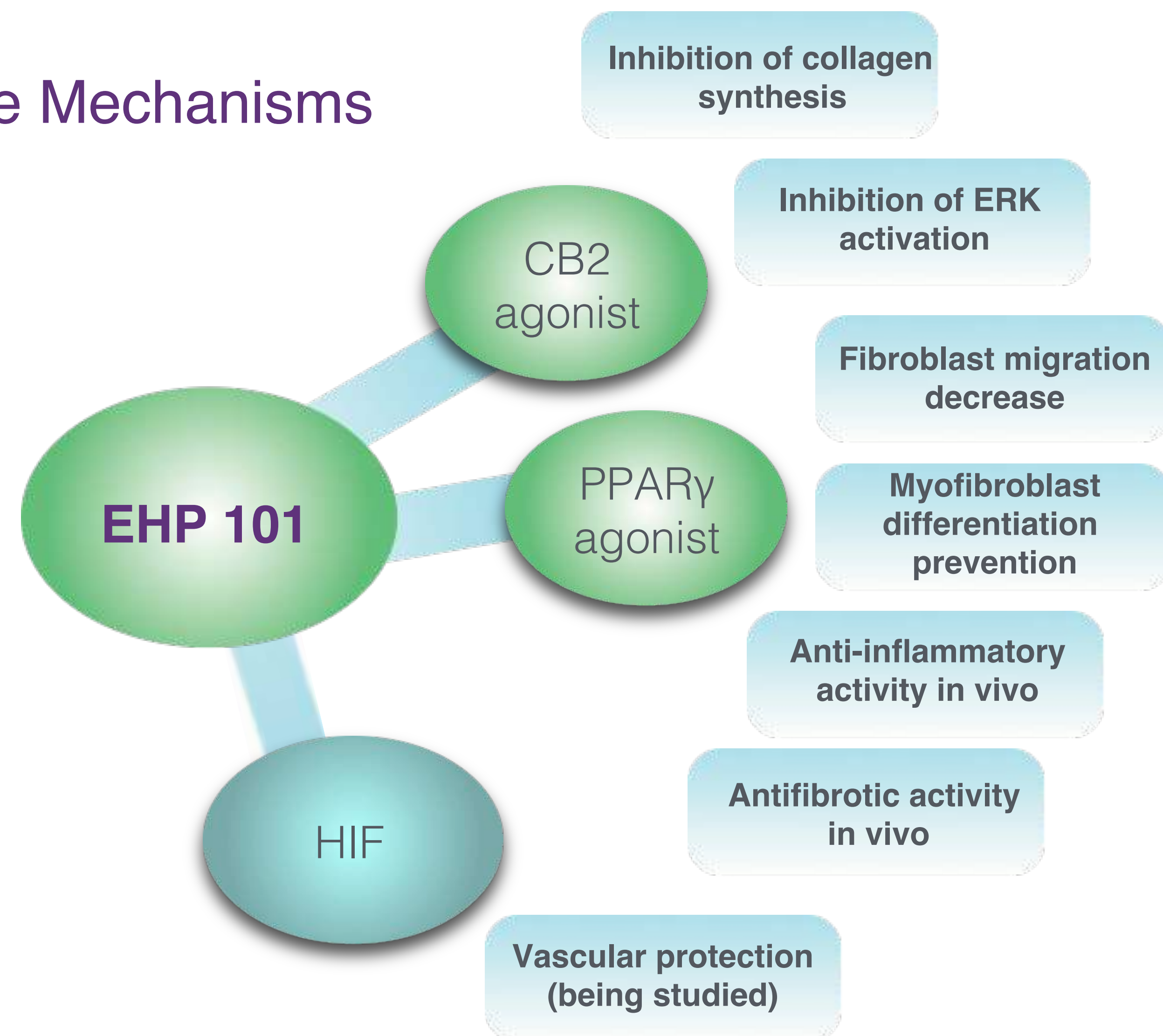
Nature Reviews | Disease Primers



# EHP-101 Targets PPAR $\gamma$ and CB2; Affects Scleroderma Through Multiple Mechanisms

- **PPAR $\gamma$**  and **CB2**: extensively studied molecular targets for the treatment of scleroderma\*
- Combined effect on PPAR $\gamma$ , CB2 and HIF not described for other types of marketed drugs
- Scleroderma is an orphan disease (no approved drugs; no cure)

\*Minghua et al, Tavarares et al, Akhmetshina et al, Del Rio et al





# EHP-101: Regulatory Plan and Timeline

**2017**

- H1** Initiated GLP tox studies and manufacturing for Phase I
- H2** US FDA grant of Orphan Drug Designation (ODD) for systemic scleroderma (SSc)  
EU EMA grant of ODD for SSc

**2018**

- H1** Final clinical-enabling studies to be completed  
Pre-IND meeting planned with US FDA (for Phase II preparation)
- H2** Phase 1 human study planned in Australia  
(single Phase I study expected to support Phase II in both MS & scleroderma)

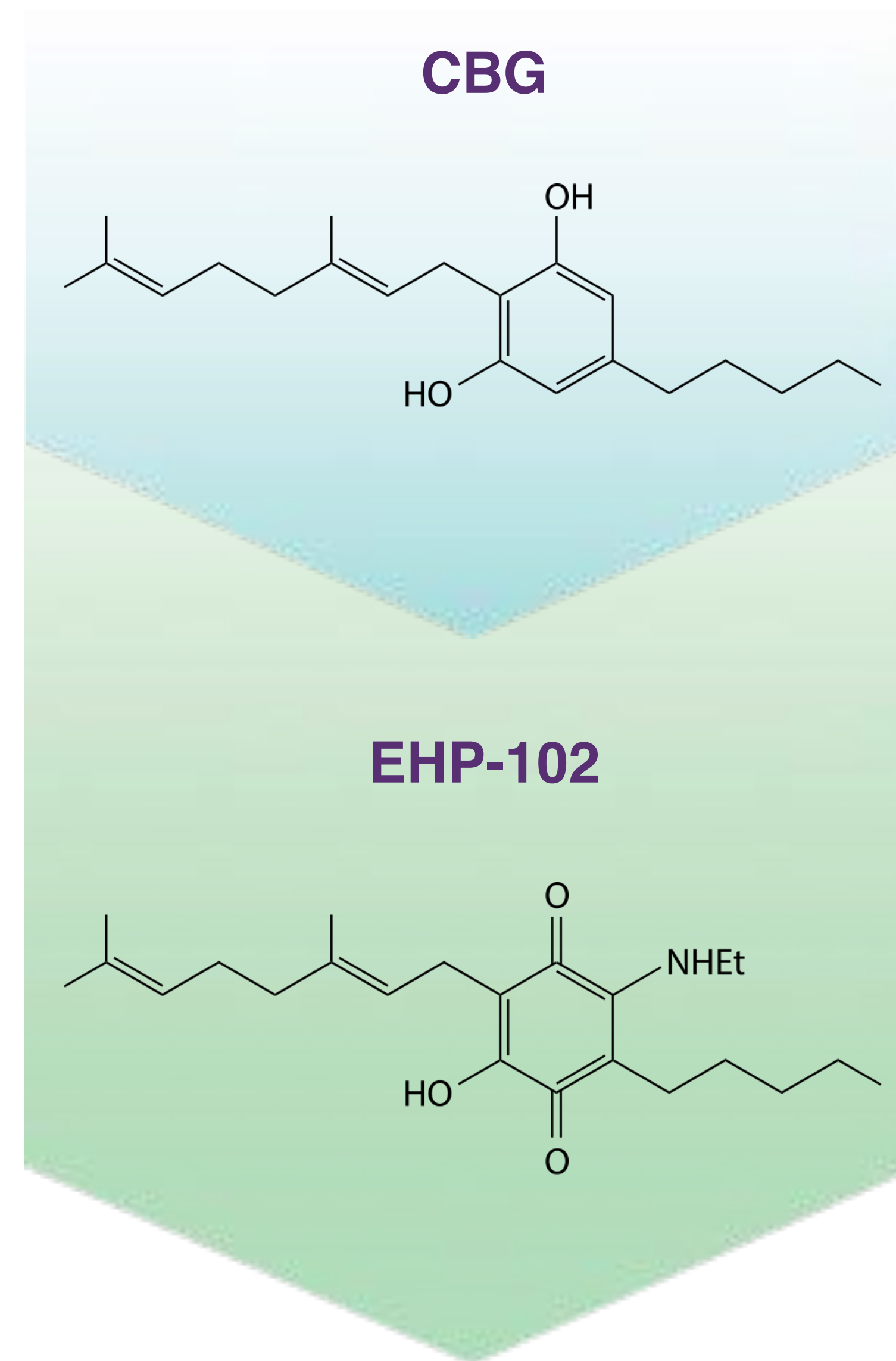


## EHP-102: Second Product Candidate

### Cannabigerol (CBG) derivative

#### CBG:

- Does not bind to CB1 (non-psychotropic)
- Provides neuroprotection in models of Huntington's disease, partially through antioxidant and anti-inflammatory activity, and PPAR $\gamma$  modulation
- Suppresses norepinephrine, providing muscle relaxation and analgesic properties through effects on the CNS

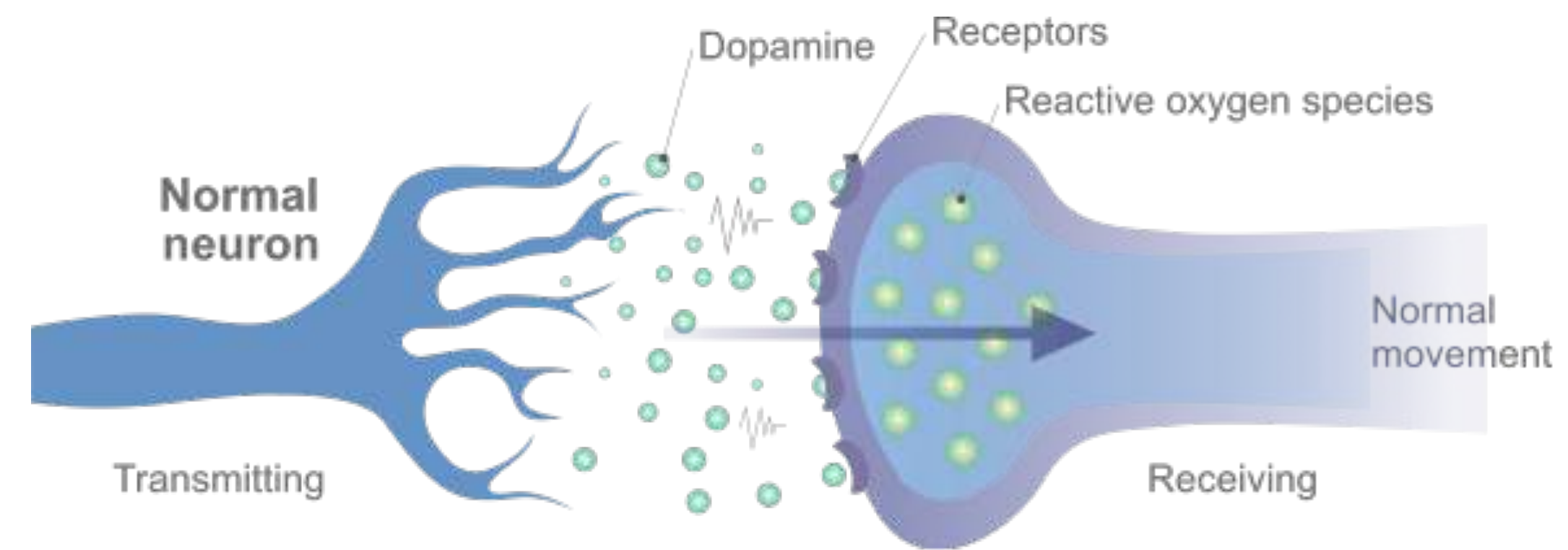




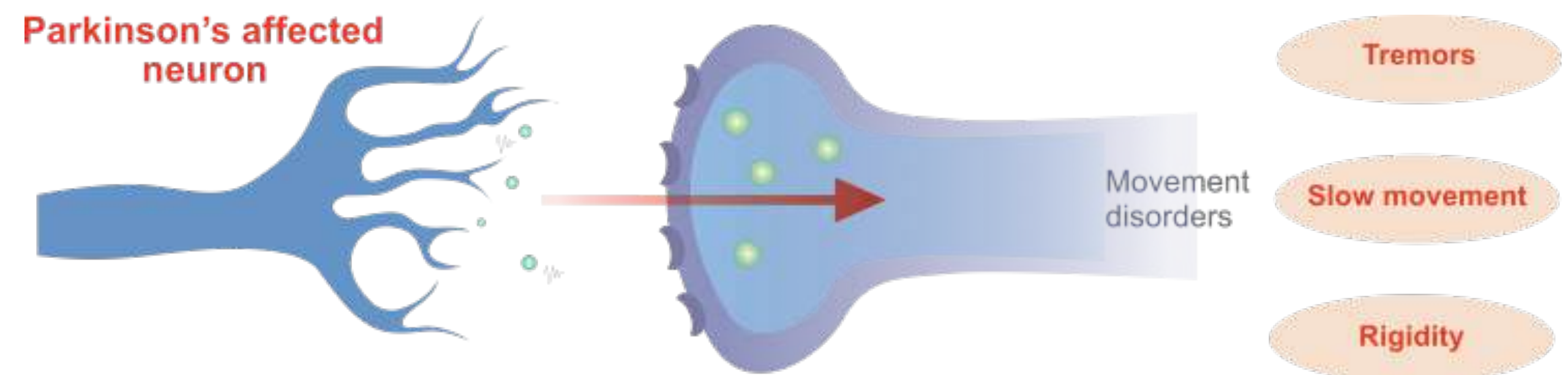
## EHP-102: Parkinson's Disease

### Chronic, progressive neurodegenerative disorder with no current cure

- More than 10 million people worldwide have Parkinson's disease
- A disease where damaged neurons do not produce sufficient dopamine (dopamine helps transmit impulses from the brain to the muscles)



Parkinson's Disease is a chronic, progressive neurodegenerative disorder with no current cure



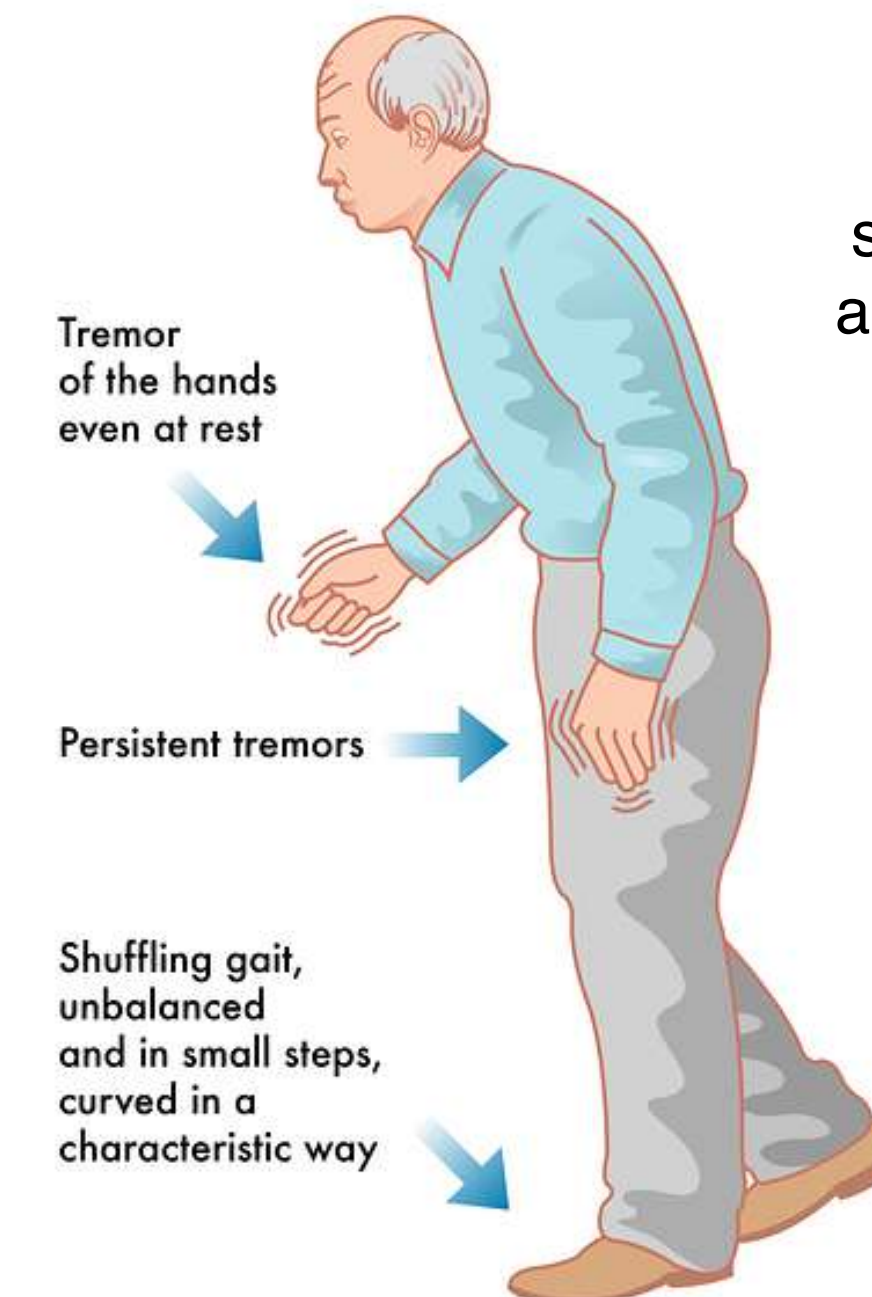
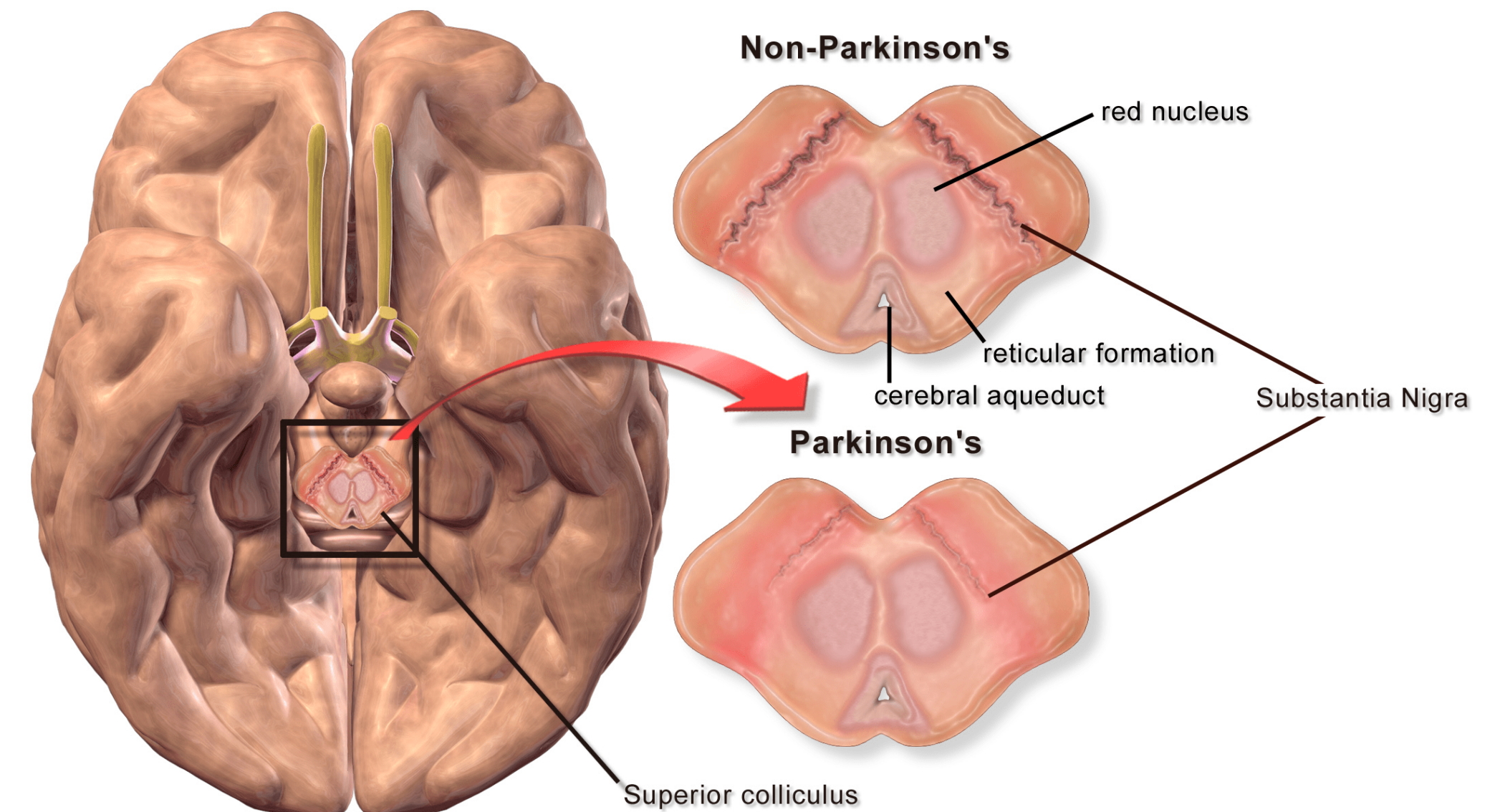


# EHP-102: Parkinson's Disease

## Parkinsons Disease

### Demonstrated efficacy in mouse models

- Provides neuroprotection, partially through PPAR $\gamma$  activity and reduction in proinflammatory mediators
- Improves clinical symptoms and recovers movement parameters (motor coordination and activity)
- Reduces inflammatory marker expression and prevents dopaminergic neuronal loss



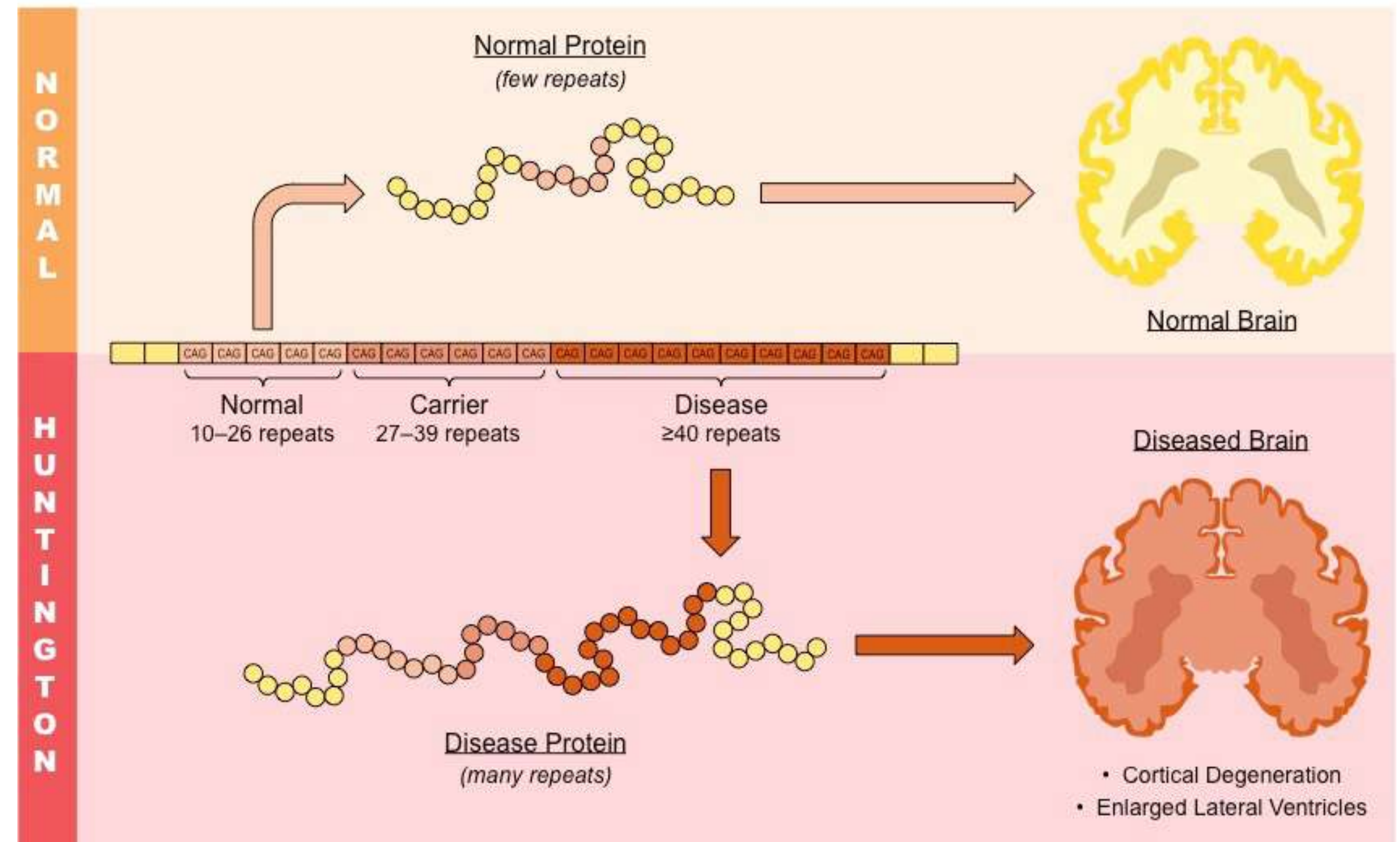
Symptoms include shaking, rigidity, slowness of movement, and difficulty with walking



## EHP-102: Huntington's disease

Causes progressive breakdown of nerve cells

- An orphan disease
- EHP-102 Targets PPAR $\gamma$  with improved activity
- Also targets other pathways involved in neural survival (ERK 1+2)







# EHP-102: Current Status

## Demonstrated preclinical efficacy





Publications

NATURE  
SCIENTIFIC

OPEN

Received: 09 October 2015  
Accepted: 29 January 2016  
Published: 18 February 2016

**The cannabinoid alleviates bleomy scleroderma and antifibrotic effect peroxisome proliferator receptor- $\gamma$  and C**

Carmen del Río<sup>1</sup>, Carmen Navarrete<sup>2</sup>, Juan A. Gómez-Cañas<sup>3,4,5</sup>, M. Ruth Pazos<sup>3,4,5</sup>, Javier I. Giovanni Appendino<sup>6</sup>, Marco A. Calzado<sup>1</sup>, Irene Cantarero<sup>5</sup>, Belén Palomares<sup>5</sup>, José Aguilera<sup>1,2,3,\*</sup>, Javier Fernández-Ruiz<sup>1,3,6</sup>, María Luz Bellido<sup>4</sup>, Federica Pollastro<sup>7</sup>, Giovanni Appendino<sup>7</sup>, Marco A. Calzado<sup>5</sup>, Ismael Galve-Roperh<sup>1,2,3</sup> & Eduardo Muñoz<sup>5</sup>

Scleroderma is a group of rare diseases associated with chronic inflammation, tissue injury, followed by fibrosis affecting the skin and internal organs. Fibrosis is a hallmark of scleroderma, and disrupting the intra-cellular signaling pathways involved in the process to controlling fibrosis. Because of its potential role in the pathogenesis of scleroderma, both PPAR $\gamma$  and CB<sub>2</sub> receptors represent attractive therapeutic targets. We have developed a non-thiophilic and non-psychotropic cannabinoid (VCE-004.8) that behaves as a dual agonist of PPAR $\gamma$  and CB<sub>2</sub> receptors. VCE-004.8 inhibited TGF $\beta$ -induced Col1A2 gene transcription and collagen synthesis. Moreover, VCE-004.8 inhibited TGF $\beta$ -mediated myofibroblast differentiation and impaired wound-healing activity. The anti-fibrotic efficacy *in vivo* was investigated in a murine model of dermal fibrosis induced by bleomycin. VCE-004.8 reduced dermal thickness, blood vessels collagen accumulation and prevented mast cell degranulation and macrophage infiltration in the skin. These effects were impaired by the PPAR $\gamma$  antagonist T0070907 and the CB<sub>2</sub> antagonist AM630. In addition, VCE-004.8 downregulated the expression of several key genes associated with fibrosis, qualifying this semi-synthetic cannabinoid as a novel compound for the management of scleroderma and, potentially, other fibrotic diseases.

NATURE  
SCIENTIFIC REPORTS

www.nature.com/scientificreports

OPEN

**VCE-003.2, a novel cannabigerol derivative, enhances neuronal progenitor cell survival and alleviates symptomatology in murine models of Huntington’s disease**

Received: 29 January 2016  
Accepted: 24 June 2016  
Published: 19 July 2016

Javier Díaz-Alonso<sup>1,2,3,\*</sup>, Juan Paraíso-Luna<sup>1,2,3,\*</sup>, Carmen Navarrete<sup>4,\*</sup>, Carmen del Río<sup>5</sup>, Irene Cantarero<sup>5</sup>, Belén Palomares<sup>5</sup>, José Aguilera<sup>1,2,3</sup>, Javier Fernández-Ruiz<sup>1,3,6</sup>, María Luz Bellido<sup>4</sup>, Federica Pollastro<sup>7</sup>, Giovanni Appendino<sup>7</sup>, Marco A. Calzado<sup>5</sup>, Ismael Galve-Roperh<sup>1,2,3</sup> & Eduardo Muñoz<sup>5</sup>

Cannabinoids have shown to exert neuroprotective actions in animal models by acting at different targets including canonical cannabinoid receptors and PPAR $\gamma$ . We previously showed that VCE-003, a cannabigerol (CBG) quinone derivative, is a novel neuroprotective and anti-inflammatory cannabinoid acting through PPAR $\gamma$ . We have now generated a non-thiophilic VCE-003 derivative named VCE-003.2 that preserves the ability to activate PPAR $\gamma$  and analyzed its neuroprotective activity. This compound exerted a prosurvival action in progenitor cells during neuronal differentiation, which was prevented by a PPAR $\gamma$  antagonist, without affecting neural progenitor cell proliferation. In addition, VCE-003.2 attenuated quinolinic acid (QA)-induced cell death and caspase-3 activation and also reduced mutant huntingtin aggregates in striatal cells. The neuroprotective profile of VCE-003.2 was analyzed using *in vivo* models of striatal neurodegeneration induced by QA and 3-nitropropionic acid (3NP) administration. VCE-003.2 prevented medium spiny DARPP32<sup>+</sup> neuronal loss in these Huntington’s-like disease mice models improving motor deficits, reactive astrogliosis and microglial activation. In the 3NP model VCE-003.2 inhibited the upregulation of proinflammatory markers and improved antioxidant defenses in the brain. These data lead us to consider VCE-003.2 to have high potential for the treatment of Huntington’s disease (HD) and other neurodegenerative diseases with neuroinflammatory traits.

García et al. *Journal of Neuroinflammation* (2018) 15:19  
DOI 10.1186/s12974-018-1060-5

Journal of Neuroinflammation

RESEARCH Open Access

**Benefits of VCE-003.2, a cannabigerol quinone derivative, against inflammation-driven neuronal deterioration in experimental Parkinson’s disease: possible involvement of different binding sites at the PPAR $\gamma$  receptor**

Concepción García<sup>1,2,3</sup>, María Cristina Palomo-Garó<sup>1,2,3</sup>, Sara Valdeolivas<sup>1,2,3</sup>, M. Luz Bellido<sup>8</sup>, Moisés García<sup>1,2,3</sup> and Javier Fernández-Ruiz<sup>1,2,3</sup>

**Abstract**  
**Background:** Neuroprotective compounds with antioxidant or anti-inflammatory properties and neuroprotective properties are needed for the treatment of Parkinson’s disease. Cannabigerol (CBG), which is a non-psychotropic cannabinoid, is also an antioxidant and neuroprotective compound. We evaluated the neuroprotective properties of VCE-003.2, a cannabigerol quinone derivative, in a (LPS) model of PD, as well as in a model of PD generated from PPAR $\gamma$  receptor was fully activated and sustained with treatment. (Continued on next page)

Journal of Neuroinflammation

**Hypoxia mimetic activity of VCE-004.8, a cannabidiol quinone derivative: implications for multiple sclerosis therapy.**  
--Manuscript Draft--

Manuscript Number:	JNEU-D-18-00001R1
Full Title:	Hypoxia mimetic activity of VCE-004.8, a cannabidiol quinone derivative: implications for multiple sclerosis therapy.
Article Type:	Research Article

Neurotherapeutics  
DOI 10.1007/s13311-014-0304-z

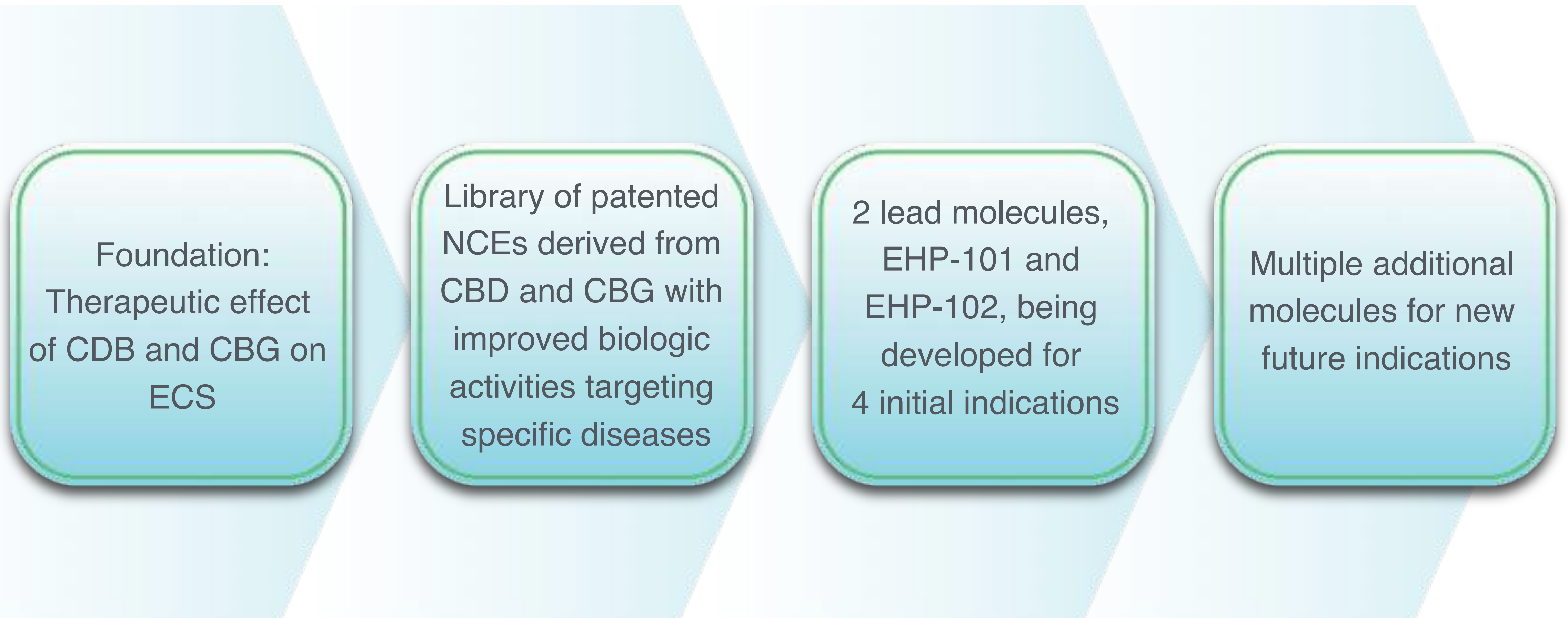
ORIGINAL ARTICLE

**Neuroprotective Properties of Cannabigerol in Huntington’s Disease: Studies in R6/2 Mice and 3-Nitropropionate-lesioned Mice**

Sara Valdeolivas • Carmen Navarrete • Irene Cantarero • María L. Bellido • Eduardo Muñoz • Onintza Sagredo



## Emerald Health Pharmaceuticals Summary







## Emerald Health Pharmaceuticals Summary

Combined MoA  
for EHP molecules  
not described with  
other drugs

EHP-101 human  
study planned for  
2018

Orphan status  
granted for  
scleroderma and  
Huntington's

Management  
team experienced  
in developing  
drugs and building  
companies



# Experienced Pharma / Biotech Management Team

**Jim DeMesa, MD, MBA**  
Chief Executive Officer

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**29 years** in pharma product development and management, including preclinical and clinical trial management, and partnering with pharma companies. 15 years as CEO of public biotech companies.

**Alain Rolland, PharmD, PhD**  
VP, Product Development

---

**30 years** of international leadership experience in R&D, strategic product management, and business development.

**Mari-Luz Bellido, PhD, MBA**  
VP, European Operations

---

Molecular biologist with **10 years** experience in preclinical development of cannabis-based compounds.

**Avtar Dhillon, MD**  
Chairman

---

Chairman of 5 public life science companies, led turnaround of NASDAQ:INO from \$10m to \$550m

**Jill Broadfoot**  
Chief Financial Officer

---

**31 years** in biotech financial management at GW Pharma (NASDAQ:GWPH), CFO, Vical (NASDAQ:VICL), Ernst & Young. BS in Business Administration and CPA.

**Nancy Coulson**  
VP, Regulatory Affairs

---

**30 years** in global pharma and biotech regulatory management with J&J, BMS, and others.

**Eduardo Muñoz, MD, PhD**  
Chief Scientific Officer

---

**30 years** in biomedical research, Professor of Immunology, author of 200 articles, patents and book chapters with nearly 5,000 citations.

**Giovanni Appendino, PhD**  
Scientific Advisor

---

One of the worlds thought leaders in cannabinoid research; Keynote speaker at the 2014 ICRS Symposium; Professor of Pharmaceutical Chemistry at the University of Eastern Piedmont; Author of 250 articles and 10 book chapters.

## Clinical Advisors:

MS: Emmanuelle Waubant, MD  
Juan-Antonio Garcia Merino, MD  
SSc: John Varga, MD  
Janet Pope, MD  
Patricia Carreira, MD





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