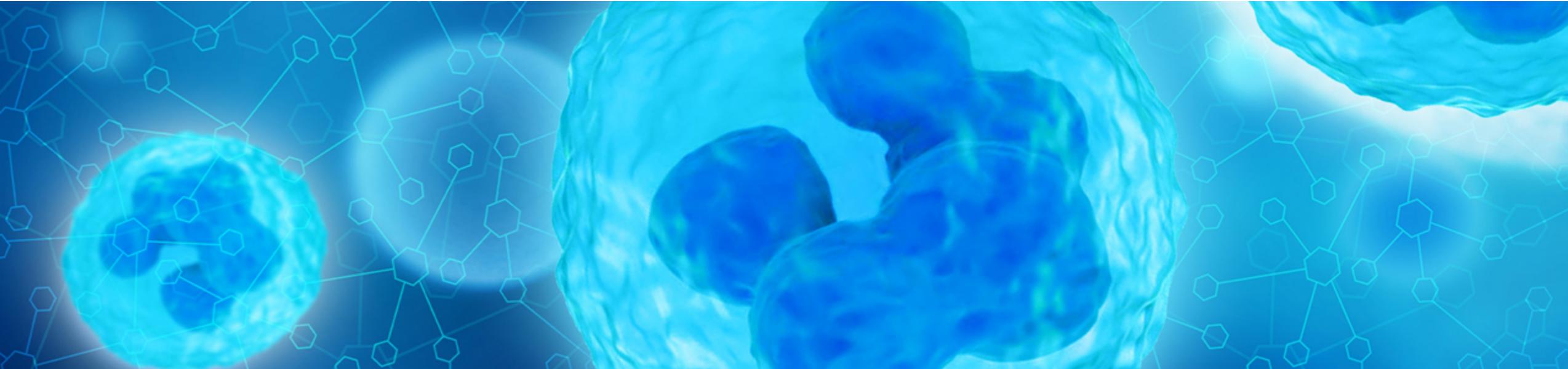


# MP1032 - First-In-Class Immunomodulator for the Treatment of Inflammatory & Infectious Diseases



# What makes MP1032 First-In-Class and Unique?

**Unique first-in-class self-regulating mechanism only activated by excessive ROS**

First and **only drug** capable of reducing **excessive ROS (reactive oxygen species)** levels back to **normal without falling below the essential physiological levels** which are required by every cell to perform specific functions

**Broad anti-inflammatory efficacy**

- Rapid antioxidative effects (**controlled ROS** scavenger activity )
- **Reduction** of inflammatory **cytokines (cytokine storm)** to **physiologic** levels (e.g. **TNF- $\alpha$** , **IL-1 $\beta$** , **IL-6**, **IL-12 & IL-23**)
- Inhibition of **PARP-1** (poly ADP-ribose polymerase 1) reduces inflammatory cytokines

**Host-directed anti-infectious efficacy**

- Immuno-mediated **reduction of viral replication** (e.g. **SARS-CoV-2**, **respiratory syncytial virus and influenza**)
- Immuno-mediated **anti-bacterial effects** (e.g. **sepsis**, **peritonitis**, **multi-drug-resistant bacteria**)

**Excellent safety (no immunosuppression)**

- **Dose-limiting toxicity** could **never** be reached in preclinical studies
- **No drug-related serious adverse events** in 4 clinical trials (**234 participants treated with MP1032**)
- **Fewer TEAEs in 2 treatment groups** compared to **placebo group (CT04, 155 patients)**

# What Are Reactive Oxygen Species (ROS) and Why Do They Matter?

- ROS (Reactive Oxygen Species)
  - Chemically reactive oxygen-containing molecules



- Every cell **needs ROS at physiological (low/moderate)** levels for
  - Cell signaling
  - Immune defense
  - Adaptation to exercise

⇒ If ROS are **below physiological levels**, the above **cell functions cannot be executed**



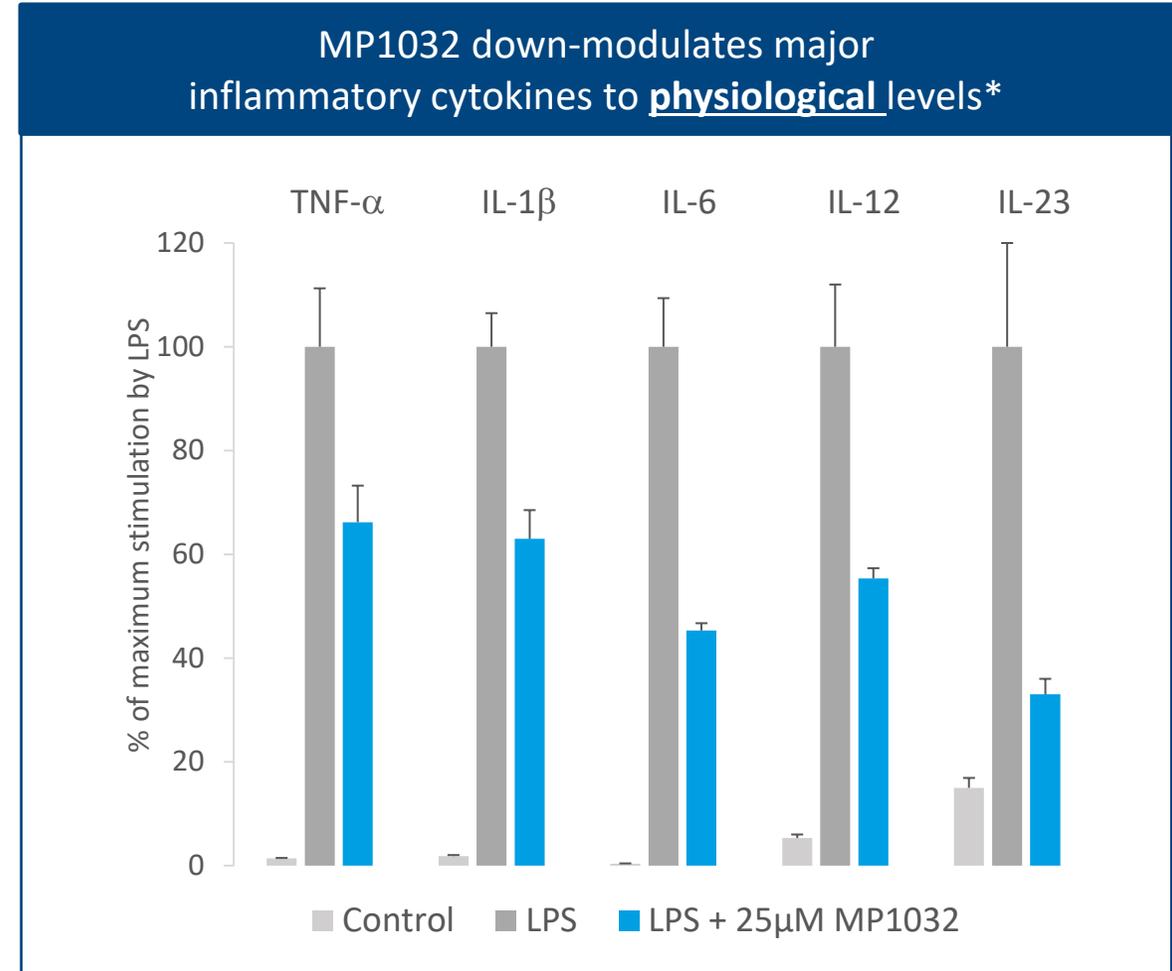
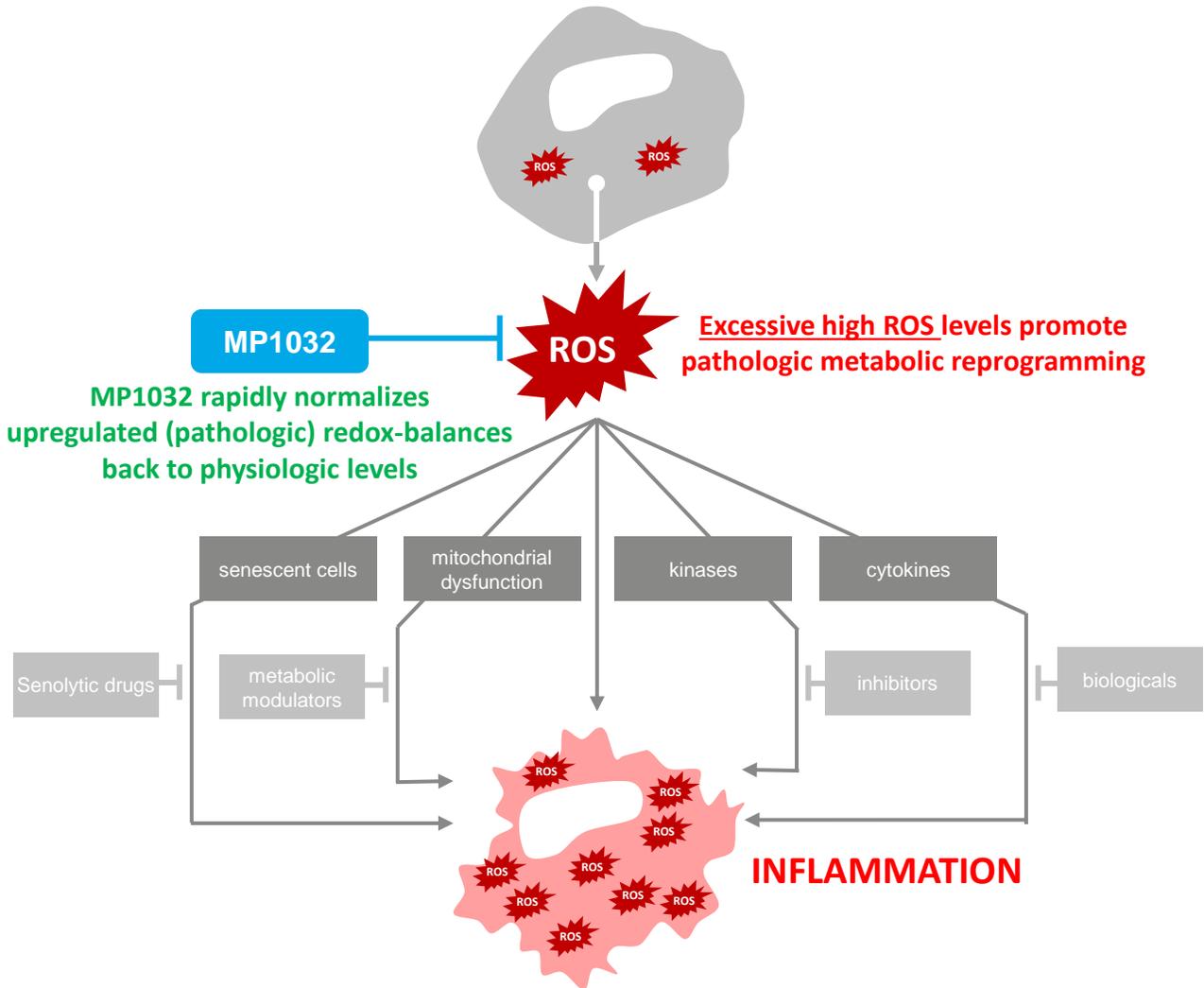
- However, **excessive (too high)** levels of ROS:
  - Trigger chronic inflammation
  - Disrupt mitochondria
  - Damage proteins, lipids, DNA
- **Problem:** Reduction of ROS **cannot stop at physiological levels (but fall below)** -> **severe side effects**



- MP1032 is **not active at physiological ROS level** but gets **activated only at excessive ROS concentrations**
  - ⇒ thereby **MP1032 reduces excessive ROS** back to **physiological (non-damaging)** level
  - ⇒ **without causing ROS to fall below** the **essential physiological levels** required by every cell to perform specific functions



# MP1032 has Positive Effects Upstream of Multiple inflammatory Pathways Thereby Enhancing the Efficacy of Other Anti-Inflammatory Therapeutics

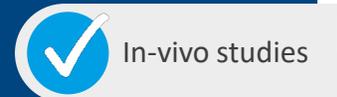


\* in primary mouse macrophages; LPS: lipopolysaccharides

# Anti-Inflammatory Efficacy of MP1032 Demonstrated in Preclinical and Clinical Studies

## Focus on Steroid Sparing

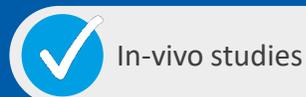
- **Similar efficacy to corticosteroids** (“Cortisone”) demonstrated in several in vivo models for
    - **Duchenne muscular dystrophy** (orphan drug designation in the US & EU, rare pediatric disease designation)
    - **Multiple sclerosis**
  - **Boost of corticosteroid anti-inflammatory potency** by **synergistic effects** with Prednisolone
- **Steroid sparing/replacement** potential with **higher efficacy** and **fewer side effects**



### Rheumatoid Arthritis

Demonstrated **efficacy (arthritic score) comparable to the TNF $\alpha$ -inhibitor Etanercept (Enbrel<sup>®</sup>)**

**Steroid sparing option**



### Duchenne Muscular Dyst.

Improved **maximal muscle force** compar. to prednisolone. **Improvement in muscle performance** in *mdx* mice

**Steroid sparing opt.**



### Sepsis

**Outstanding efficacy** in preclin. models; **100% survival rate** and **full recovery within 3 days** in treatment group with MP1032



### Multiple Sclerosis

**Efficacy comparable to Dexamethasone. Better efficacy** than leading MS drug (Tecfidera<sup>®</sup> /DMF)

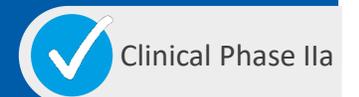
**Steroid sparing option**



### Psoriasis

Disease modifying activity & **fewer TEAEs in 2 treatment groups than placebo** in Ph. II study w. 155 patients

**Steroid sparing option**



# Anti-infectious Host-mediated Efficacy of MP1032

## COVID-19

- Excellent results in Phase IIa study with **132 hospitalized patients**
- Funded by **€7.9m EU-grant** and results published in **LANCET Europe**
- MP1032 was given in addition to **standard of care (SOC)**, resulting in
  - **Reduced hospital days** on average **by 2.5 days\***
  - **Reduced ICU days** on average **by 4 days\***

\*numerically



Clinical Phase-IIa

## Multiple Virus Variants of SARS-CoV-2

- Consistent **anti-viral effect independent** of virus variant
- Reduced SARS-CoV-2 viral replication (dose dependently)
  - Wuhan Type
  - Alpha Variant
  - Beta Variant
  - Gamma Variant
  - Delta Variant
  - Omikron Variant



In vitro studies

## Long COVID Potential

- MP1032 shows **efficacy against 4 cardinal drivers** of Long COVID
  - Fights persistent virus
  - Normalization of persistent immune dysregulation
  - Prevention of micro-embolisms
  - Inhibits pulmonary fibrosis



Scientific Rationale

## Anti-bacterial Effects in Various Organs

- MP1032 **significantly reduces bacterial load** in the blood, peritoneal lavage, liver and lungs after 12 hours
- This marked **anti-bacterial effect** was mediated by the **modulation** of the **redox balance** of immune cells
- Redox metabolic modulation is a **highly promising approach to treat bacterial infections** including **antibiotic-resistant strains**



In vivo studies

# Outstanding Safety Demonstrated in Pre-Clinical and Clinical Trials

## Pre-clinical

-   Max. oral dosing  
16 x human dose  
6 months  
*No dose-limiting toxicity could be reached*
-   Max. oral dosing  
14 x human dose  
12 months  
*No observed adverse effect*
-   Max. oral dosing  
Up to 32 x human dose  
*No adverse effects on fertility and embryonic-fetal development*

## Clinical

### Phase 1

-   Max. oral repeat dose  
600 mg  
*No safety issues detected*

### Phase 2a Psoriasis

-   Max. oral repeat dose  
200 mg  
*No safety issues detected*

### Phase 2 Psoriasis

-   Max. oral repeat dose  
600 mg  
*No safety issues detected*

### Phase 2a COVID-19

-   Max. oral repeat dose  
600 mg  
*No safety issues detected*



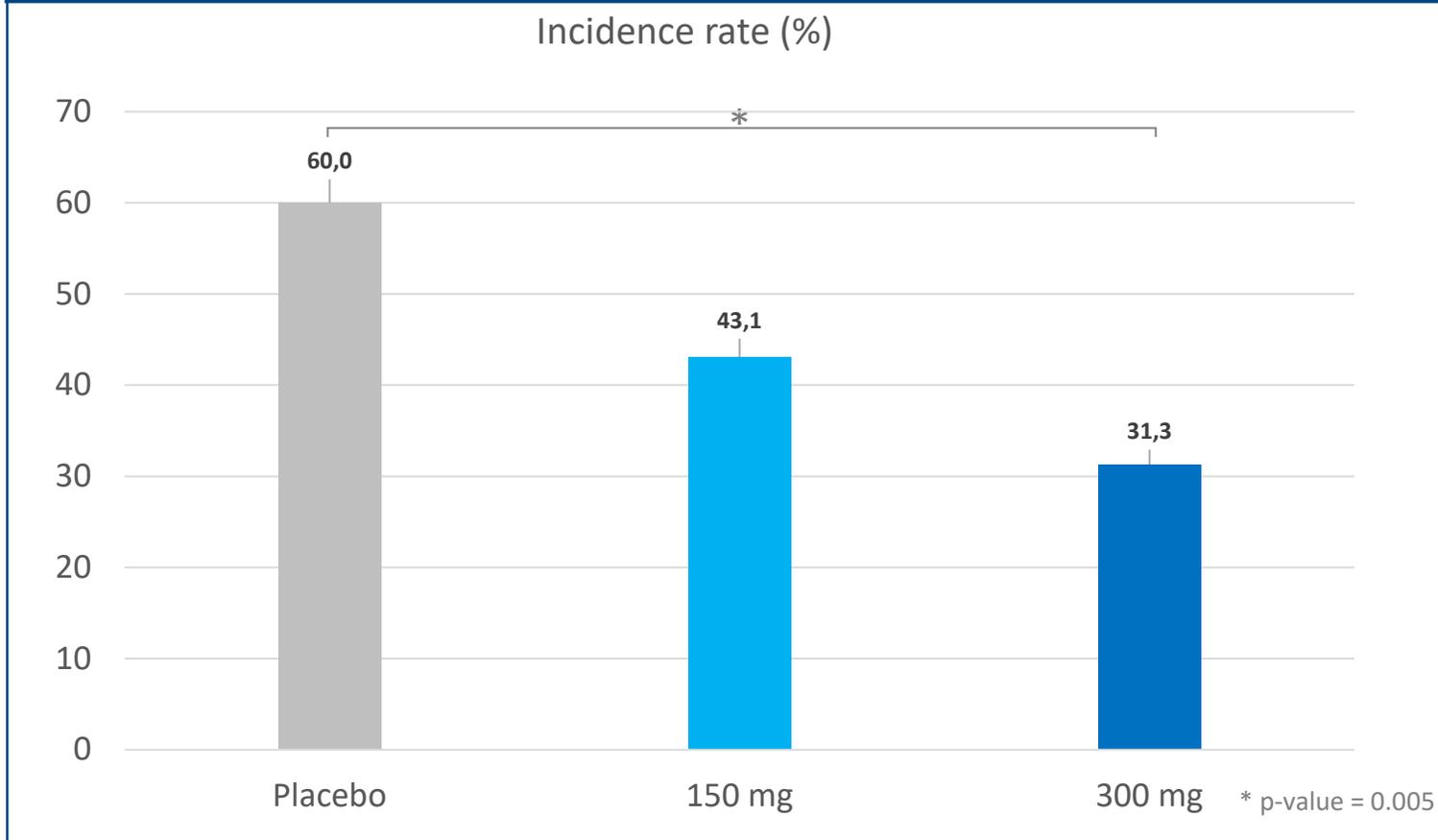
*In total, 4 clinical trials with 366 participants thereof 234 participants treated with MP1032 and 132 participants in the placebo groups*

# Less TEAEs in Treatment Groups than in Placebo Group

MP1032 Reduces Non-Drug-Related Adverse-Events in a Dose-Dependent Manner

## Phase II Safety Data (Plaque Psoriasis)

Incidence of Treatment Emergent Adverse Events (TEAEs, non drug-related)



Safety data from Phase II clinical trial MP1032-CT04 with 155 later stage plaque psoriasis patients

**155 patients; 3 months daily oral**

55 placebo b.i.d.

52 150 mg b.i.d.

48 300 mg b.i.d.

**No SAE in MP1032 Groups**

**Less TEAEs in 150mg and 300 mg dose groups**

SAE = Serious Adverse Event

TEAE = Treatment Emergent Adverse Events

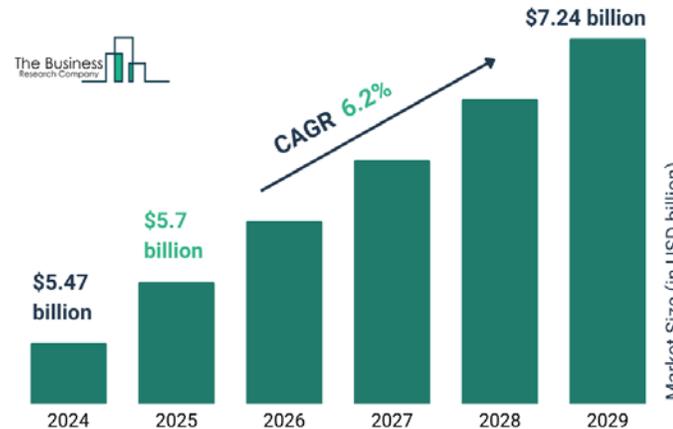
# MetrioPharm's R&D Focus: Steroid Sparing

Steroids: still the most widely used standard anti-inflammatory therapy

**But with severe side effects**

ORPHAN INDICATIONS	<p><b>Duchenne muscular dystrophy</b>                      Becker muscular dystrophy                      ANCA-associated vasculitis                      Systemic juvenile idiopathic arthritis                      Autoimmune hepatitis                      + further indications ...</p>
INDICATIONS WITH LARGE PATIENT POPULATIONS	<p><b>Rheumatoid arthritis</b>  <b>Inflammatory bowel disease</b>  <b>Multiple sclerosis</b>  <b>Psoriasis</b>  <b>COVID-19 (hospitalized)</b>  <b>Sepsis</b>  <b>COPD</b>                      Systemic lupus erythematosus                      Sarcoidosis                      Polymyalgia rheumatica                      Polymyositis                      Urticaria                      Asthma                      Interstitial lung disease                      Rhinitis                      Contact dermatitis                      + further indications ...</p>

Corticosteroids Global Market Report 2025



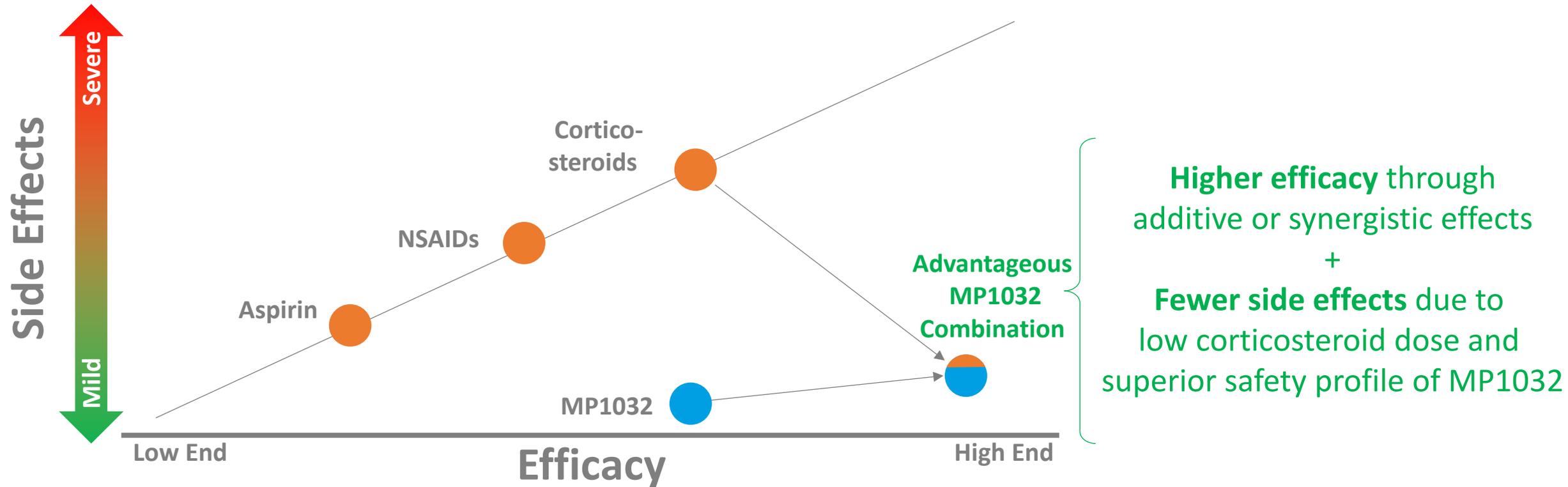
**Growth Drivers:**

- Aging
- Demographic change
- Rise in chronic diseases

- Osteoporosis**
- Muscle weakness**
- Growth suppression**
- Cushing's syndrome**
- Adrenal suppression**
- Diabetes**
- Heart damage**
- Increased susceptibility to infections (bacterial, viral, fungal)**
- Depression or psychosis**
- ...

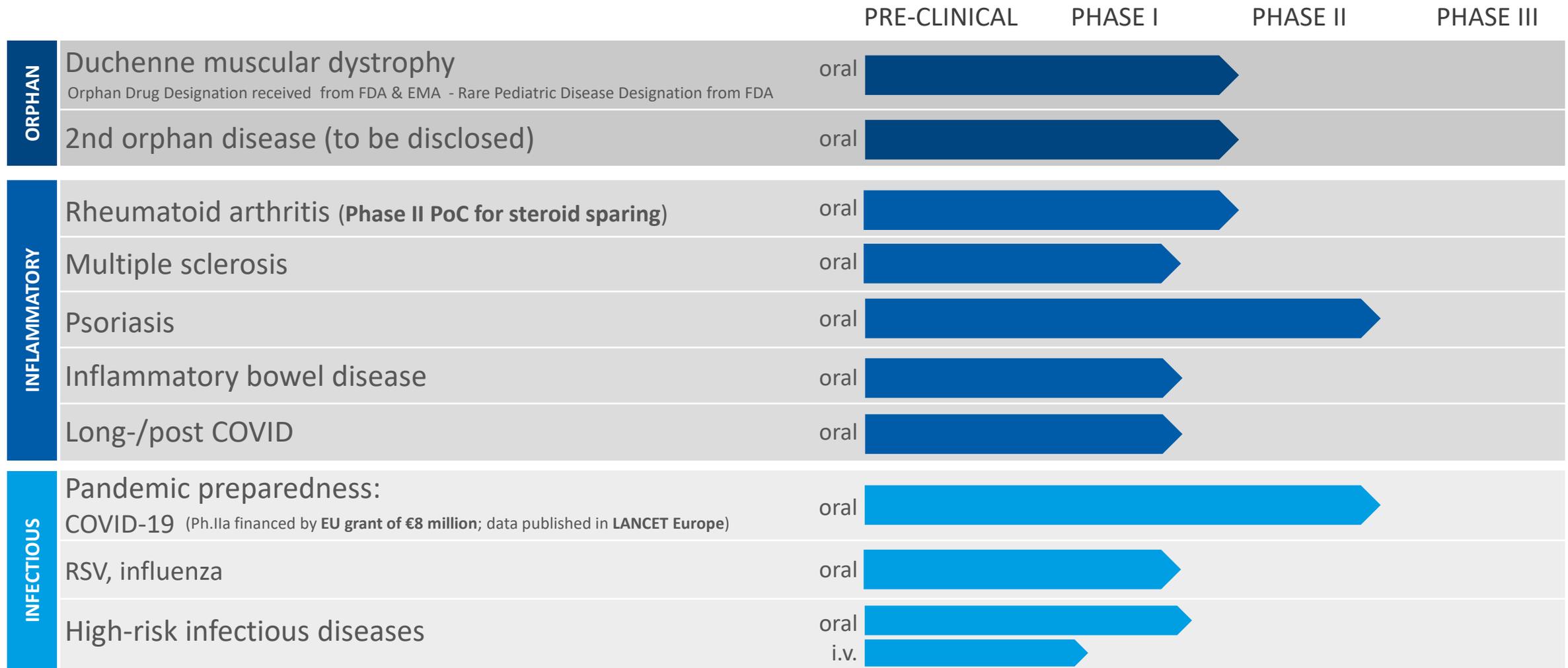
Bold indications: Preclinical/Clinical data available

# Advantages of Steroid Sparing / Replacement of MP1032



Immune Metabolic Modulation (MP1032) **boosts the efficacy** of existing anti-inflammatory drugs like corticosteroids in a **highly supra-additive way**. This allows for the creation of a **new class** of next-generation fixed-dose-combination drugs with **improved efficacies and fewer side effects from corticosteroids in a large range of indications**

# MP1032 Pipeline | Focus on Steroid Sparing & Orphan Diseases



# MetrioPharm Pipeline Targets Large Markets

Indication	Medical Need & Market Opportunity	Estimated Total Adressable Market	Estimat. Servicable Adressable Market
Rheumatoid arthritis	An effective, oral early-intervention treatment for safe long-term use	\$120.5B (2020; global) <sup>1</sup> \$163.8B (2030; global) <sup>1</sup>	\$28.9B (2023; 8MM) <sup>1</sup> \$29.1B (2029; 8MM) <sup>1</sup>
Duchenne muscular dystrophy	Steroid-sparing with improved disease-slowng properties and outstanding safety profile	\$2.3B (2023; global) <sup>1</sup> \$5.2B (2033; global) <sup>1</sup>	\$1.0B (2023; US) <sup>1</sup> \$1.8B (2033; 7MM) <sup>1</sup>
2nd orphan disease (to be disclosed)	Steroid-sparing with improved disease-slowng properties and outstanding safety profile	<i>To be disclosed</i>	<i>To be disclosed</i>
High-risk infectious diseases	Host-directed therapy for e.g. Multi drug resistant infections, Clostridioides difficile, Acute Respiratory Distress Syndrome, etc.	<i>To be disclosed</i>	<i>To be disclosed</i>
Pandemic preparedness (incl. COVID-19, RSV, influenza) & long/post COVID	A virus variant-independent oral medication for safe prophylaxis and early intervention for the next pandemic	Data not available	Data not available
Multiple sclerosis	A safer and more effective oral therapy with better tolerability compared to currently leading drugs	\$32.8B (2024; global) <sup>1</sup> \$41.28 (2034; global) <sup>1</sup>	\$22B (2024; 7MM) <sup>1</sup> \$25.9B (2034; 7MM) <sup>1</sup>
Inflammatory bowel disease	Oral maintenance therapies with higher response rates than salicylates and better safety than corticosteroids	\$23B (2023; global) <sup>1</sup> \$31.3B (2030; global) <sup>1</sup>	\$10.2B (2023; US) <sup>1</sup>
Psoriasis	A safer and more effective oral drug, especially for the large, underserved segment of mild-to-moderate psoriasis	\$31.7B (2030; 7MM) <sup>1</sup>	\$31B (2030; 7MM) <sup>1</sup>

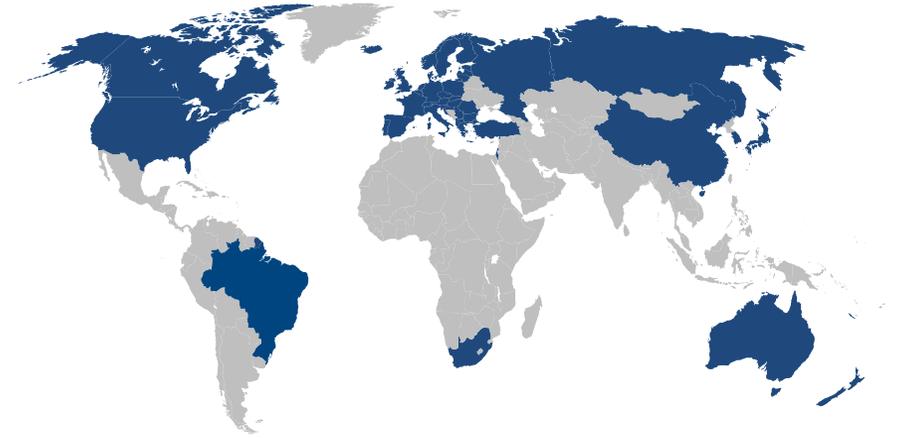
Sources: <sup>1</sup> GlobalData <sup>2</sup> AB Newswire/Delveinsight

7 Major Markets (MM): US+EU5+Japan, 8MM: US+EU5+Japan+Australia

# Intellectual Property Portfolio

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- 18 patent families including 255 granted patents to-date
- Further 100+ patent applications: potentially valid up to 2044
- Data protection and market exclusivity for orphan designation between 5 and 11 years depending on geographic region (starting with first approval)



# Investment with Social Impact



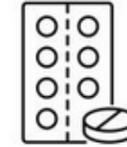
## Adresses High Medical Needs in low & middle-income countries (L&MICs)

- Affordable alternative to high-end therapies (Biologics, Cell Therapies) which are out of reach for L&MICs
- Early response to new viral threats (“Pandemic Preparedness”)
- Anti-microbial resistance



## Affordable pricing

Low cost-of-goods (manufacturing) allows for affordable pricing



## Ease of use in compromised environments

- oral
- no cooling required
- highly stable



## No need for expensive patient monitoring

Outstanding safety profile does not require extra monitoring



**Controlled distribution to L&MICs via foundations owned by large pharma companies**

# Disclaimer

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