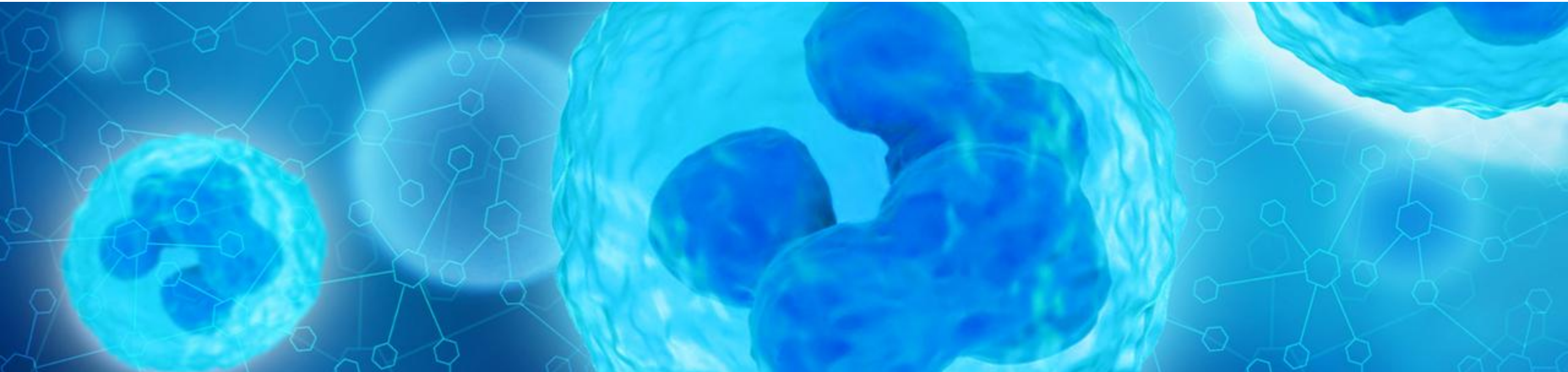


MP1032 - First-In-Class Immunomodulator for the Treatment of Inflammatory & Infectious Diseases



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** to **physiologic** levels (e.g. **TNF- α** , **IL-1 β** , **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 essential functions**
 - Cell signaling
 - Immune defense
 - Adaptation to exercise

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



- However, **excessive (too high) levels of ROS:**
 - Trigger chronic inflammation
 - Disrupt mitochondria
 - Damage proteins, lipids, DNA

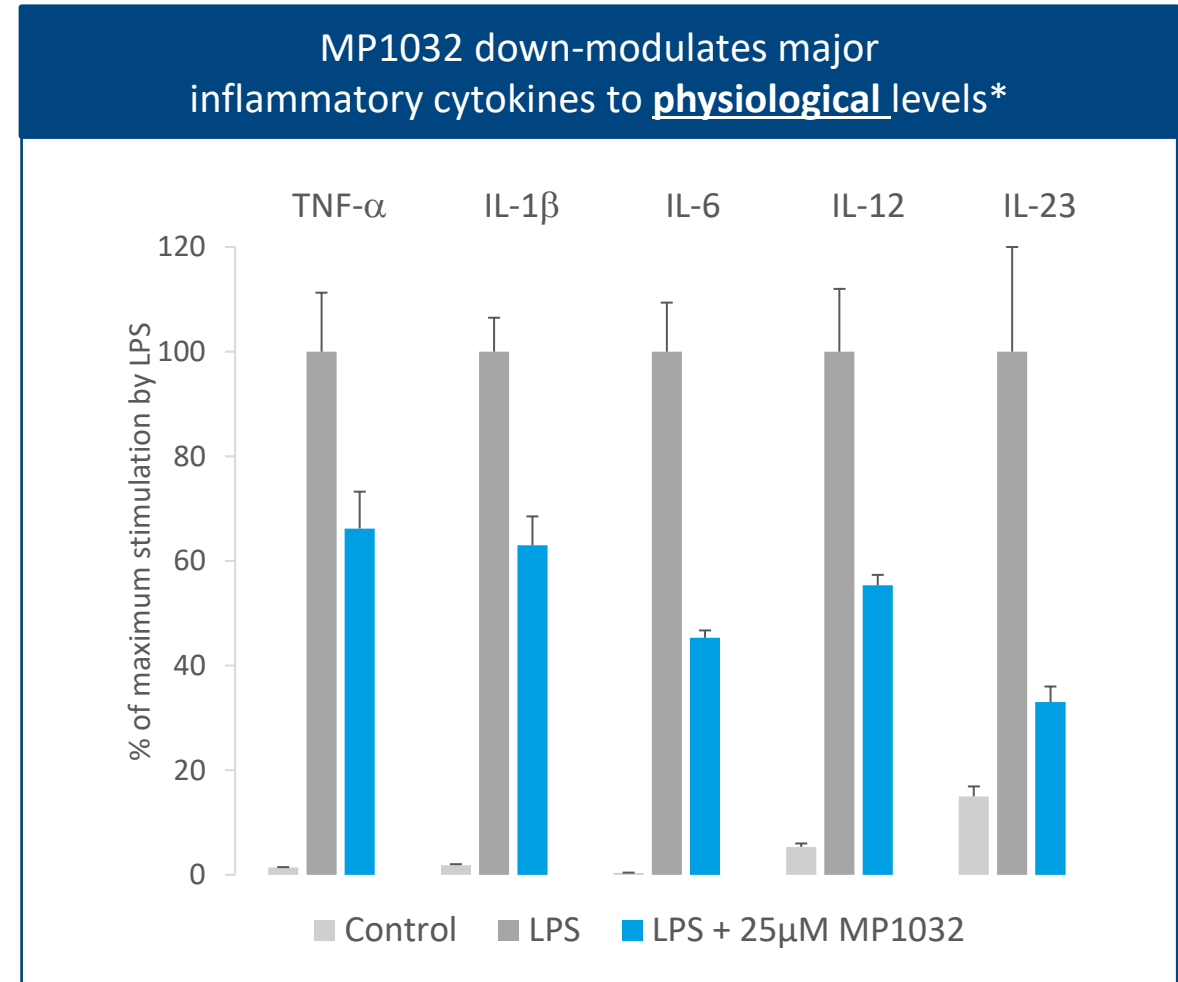
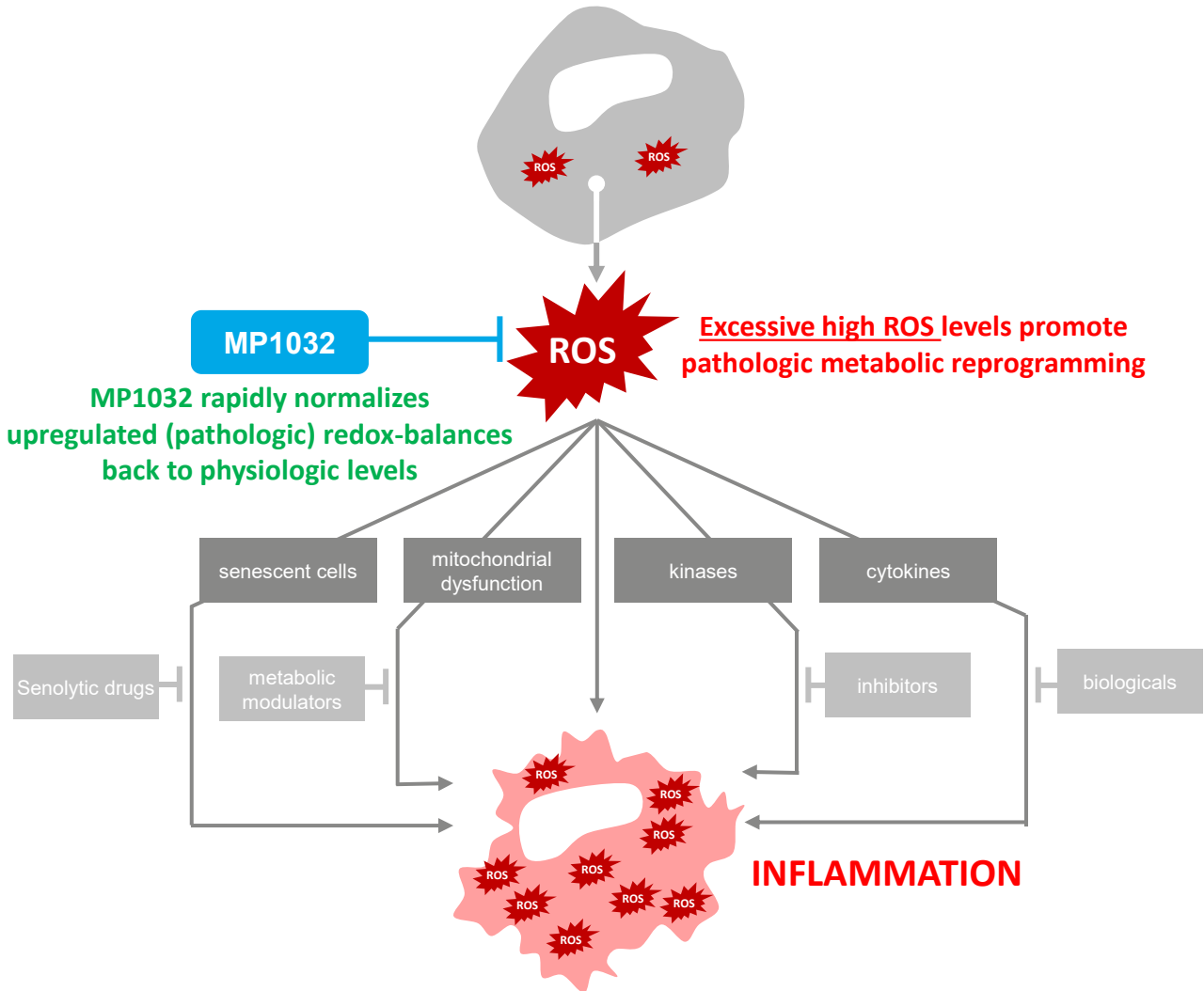


- **Problem: Reduction of ROS cannot stop at physiological levels (but fall below) -> severe side effects**

- 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

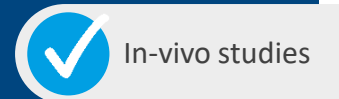


* in primary mouse macrophages; LPS: lipopolysaccharides

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

Focus on Steroid Sparing

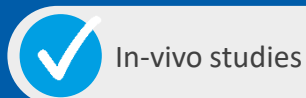
- **Similar efficacy to corticosteroids** (“Cortisone”) demonstrated in several in vivo models for
 - **Duchenne muscular dystrophy** (orphan drug designation in the US & EU, rare pediatric disease designation)
 - **Multiple sclerosis**
 - **Boost of corticosteroid anti-inflammatory potency** by **synergistic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



Rheumatoid Arthritis

Demonstrated **efficacy (arthritic score) comparable to the TNF α -inhibitor Etanercept (Enbrel®)**

Steroid & Enbrel 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® /DMF)

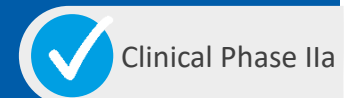
Steroid & DMF sparing option



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

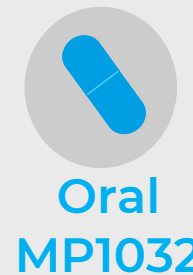
Outstanding Safety Demonstrated in Pre-Clinical and Clinical Trials

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



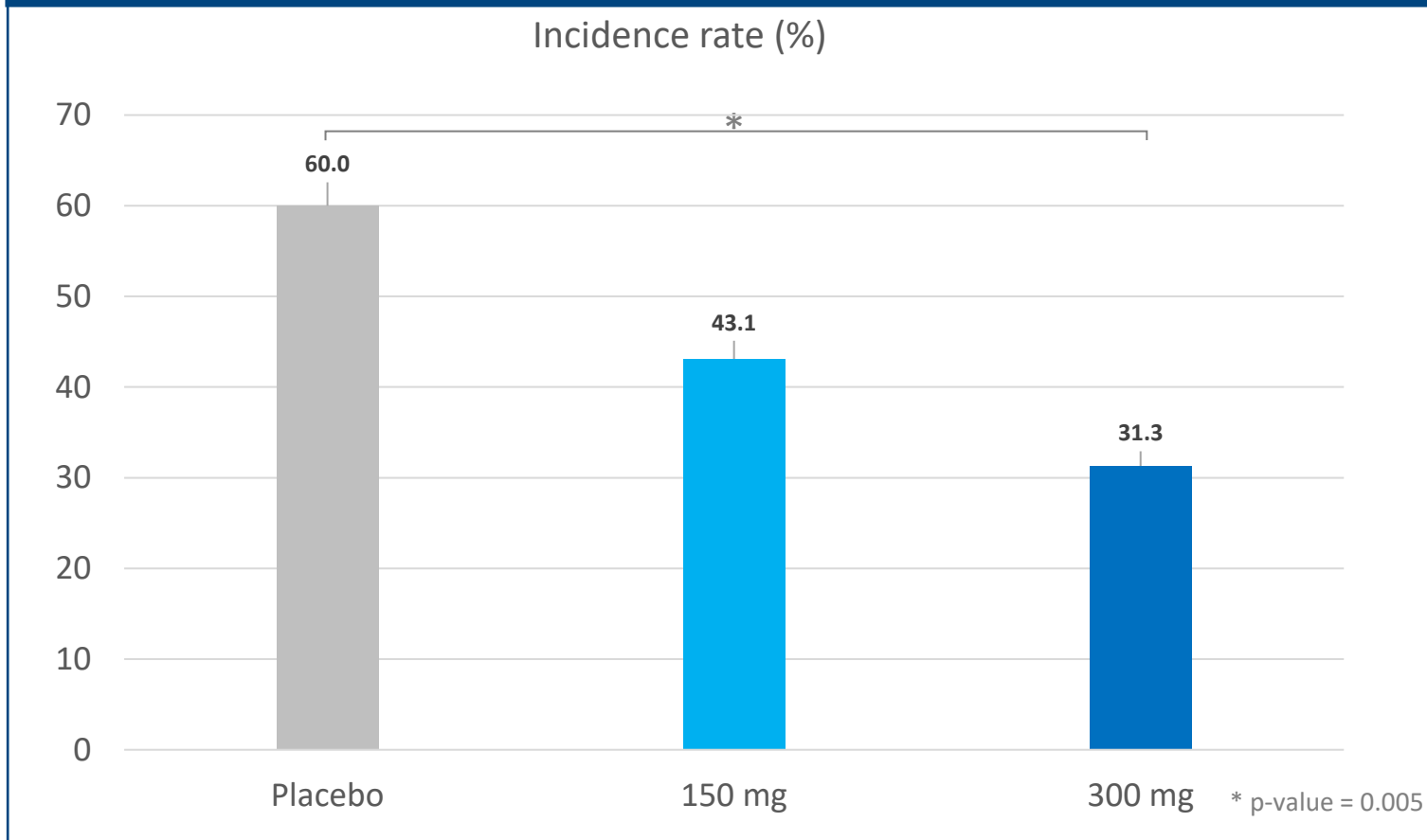
*In total, 4 clinical trials with 366 participants thereof **234 participants** treated with **MP1032** and 132 participants in the placebo groups*

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

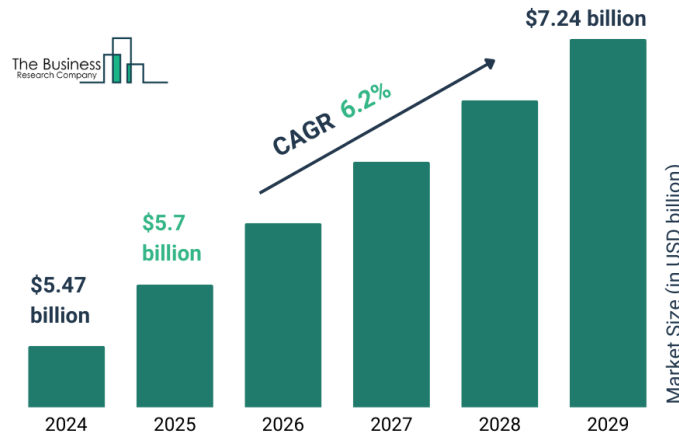
MetrioPharm's R&D Focus: Steroid Sparing

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

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

Bold indications: Preclinical/Clinical data available

Corticosteroids Global Market Report 2025



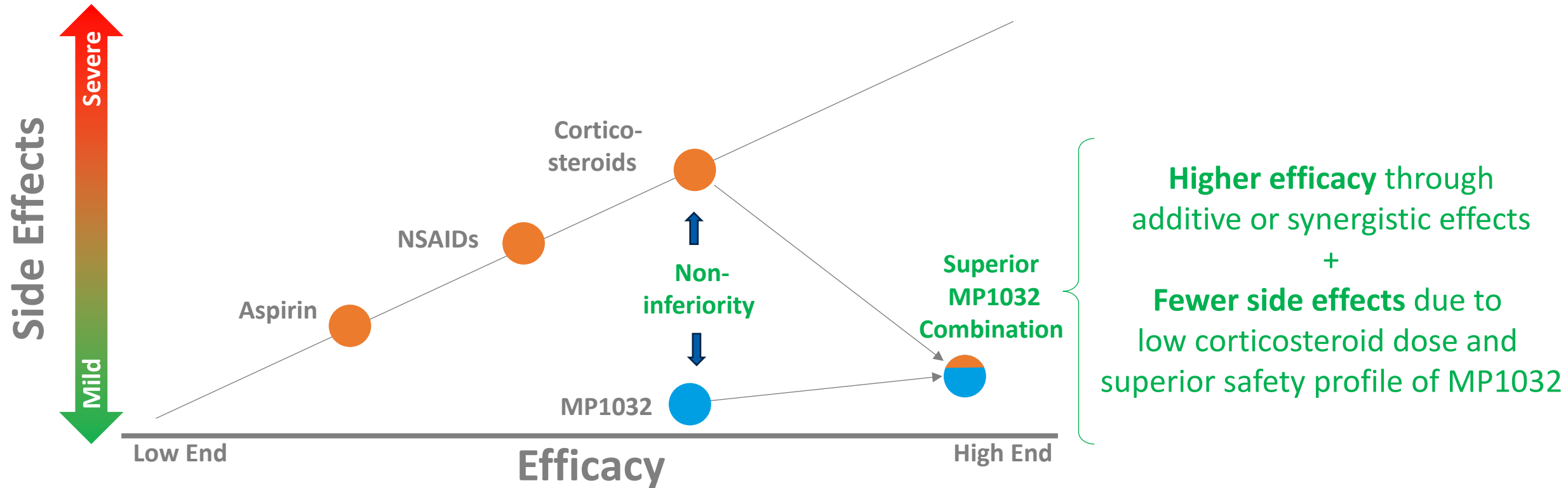
Growth Drivers:

- Aging
- Demographic change
- Rise in chronic diseases

But with severe side effects

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

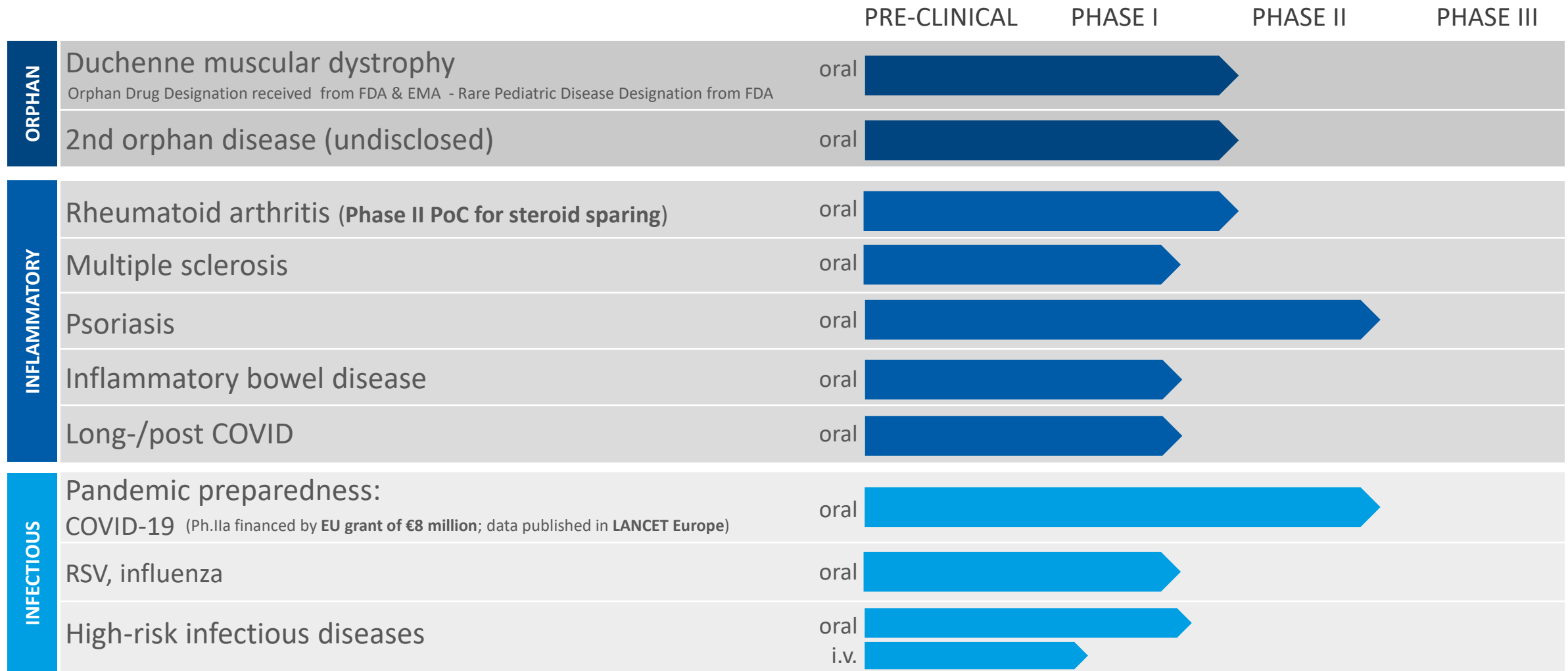
Advantages of Steroid Sparing / Replacement of MP1032



Higher efficacy through additive or synergistic effects
+
Fewer side effects due to low corticosteroid dose and superior safety profile 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

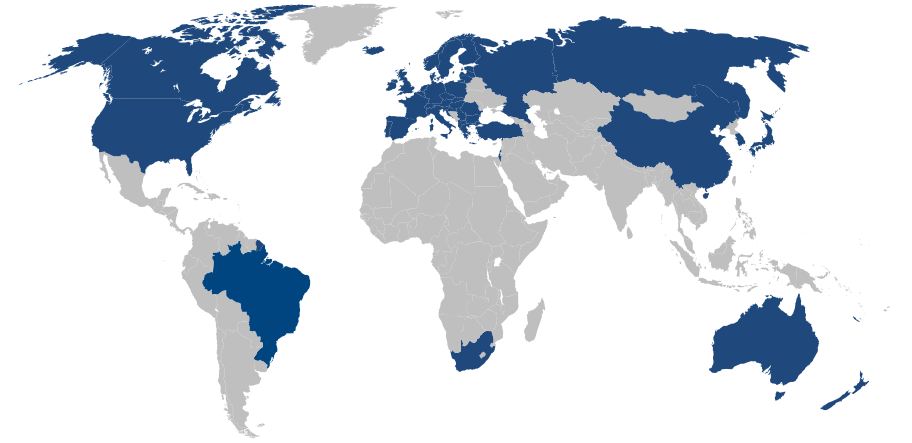
Indication	Medical Need & Market Opportunity	Estimated Total Adressable Market	Estimat. Servicable Adressable Market
Rheumatoid arthritis	An effective, oral early-intervention treatment for safe long-term use	\$120.5B (2020; global) ¹ \$163.8B [2030; global] ¹	\$28.9B (2023; 8MM) ¹ \$29.1B (2029; 8MM) ¹
Duchenne muscular dystrophy	Steroid-sparing with improved disease-slowng properties and outstanding safety profile	\$2.3B (2023; global) ¹ \$5.2B (2033; global) ¹	\$1.0B (2023; US) ¹ \$1.8B (2033; 7MM) ¹
2nd orphan disease (undisclosed)	Steroid-sparing with improved disease-slowng properties and outstanding safety profile	<i>undisclosed</i>	<i>undisclosed</i>
High-risk infectious diseases	Host-directed therapy for e.g. Multi drug resistant infections, Clostridioides difficile, Acute Respiratory Distress Syndrome, etc.	<i>undisclosed</i>	<i>undisclosed</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) ¹ \$41.28 (2034; global) ¹	\$22B (2024; 7MM) ¹ \$25.9B (2034; 7MM) ¹
Inflammatory bowel disease	Oral maintenance therapies with higher response rates than salicylates and better safety than corticosteroids	\$23B (2023; global) ¹ \$31.3B (2030; global) ¹	\$10.2B (2023; US) ¹
Psoriasis	A safer and more effective oral drug, especially for the large, underserved segment of mild-to-moderate psoriasis	\$31.7B (2030; 7MM) ¹	\$31B (2030; 7MM) ¹

Sources: ¹ GlobalData ² AB Newswire/Delveinsight

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

Intellectual Property Portfolio

- 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



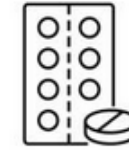
Adresses High Medical Needs in low & middle-income countries (L&MICs)

- 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

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