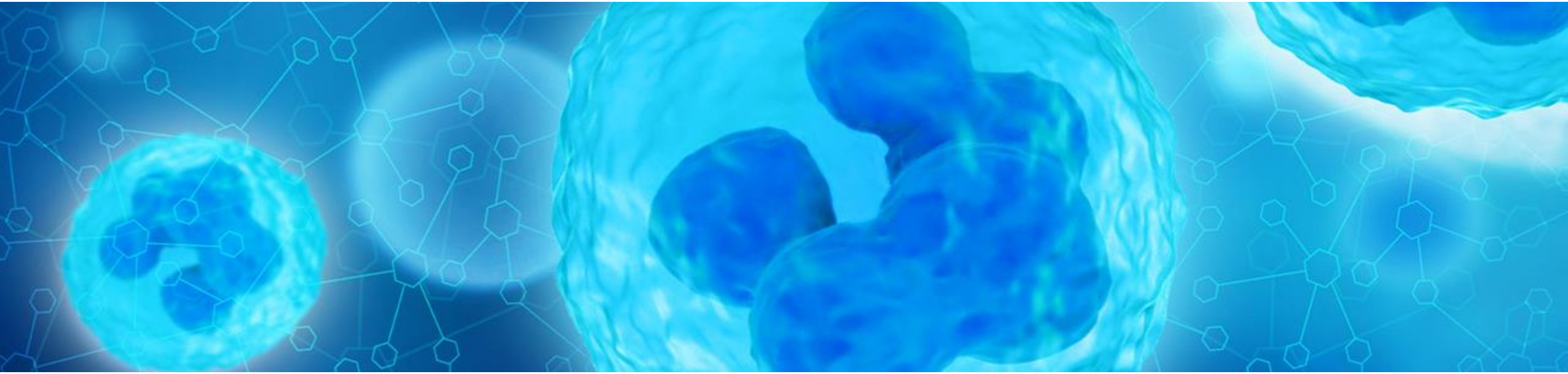
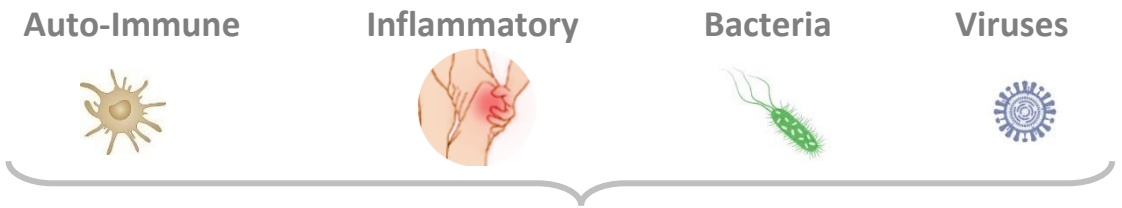
MetrioPharm

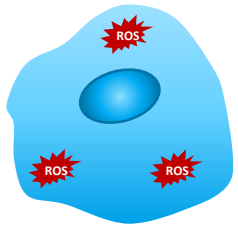


Platform of Immunomodulators Targeting the Mitochondrial Metabolism in Macrophages for Treatment of Inflammatory & Infectious Diseases

MP1032 Modulates the Mitochondrial Energy Metabolism of Macrophages By a First-in-Class Self-regulating Drug Mechanism

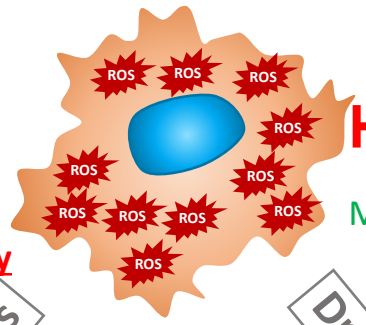
Disturbance of cell energy metabolism (=re-programming) is triggered by…





Macrophage with normal mitochondrial redox balance

Many diseases and pathogens **disrupt (re-programme) cellular/ mitochondrial energy metabolism** with significant downstream effects on driving disease pathology

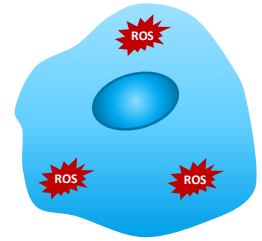


Drives

Macrophage with pathologically changed mitochondrial redox balance

Drives

MP1032's **self-regulated mechanism reverses the pathologically changed mitochondrial redox balance** back to normal



Macrophage with a normalized mitochondrial redox balance

Inflammatory Diseases

Large Indications

Psoriasis | Multiple Sclerosis | Crohn's U. Colitis | Rheumatic Diseases

Orphan

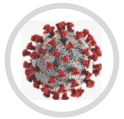
Duchenne Muscular Dystrophy | Juvenile Idiopathic Arthritis

Infectious Diseases

Bacterial

Sepsis Anti-microbial Resistance

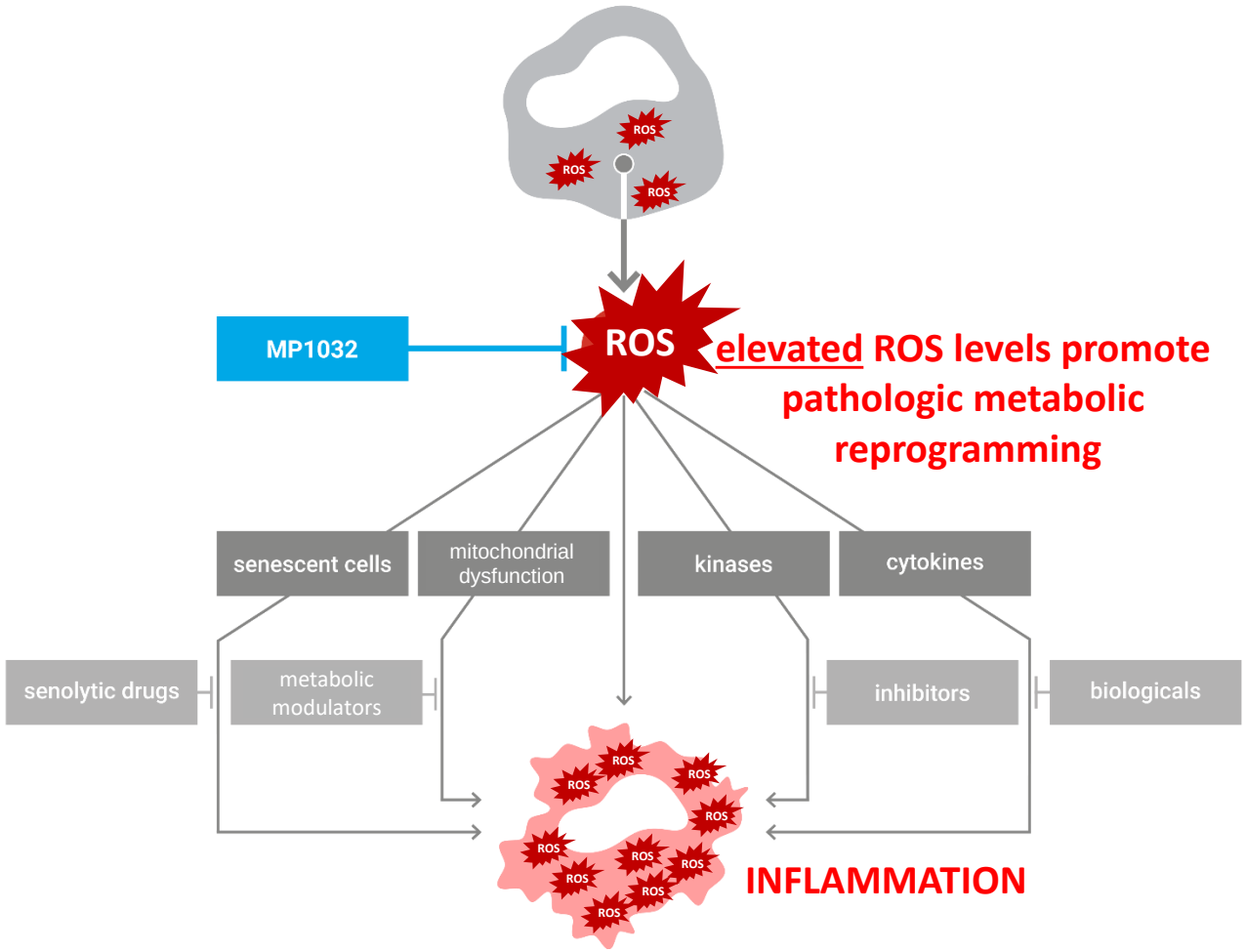
Viral



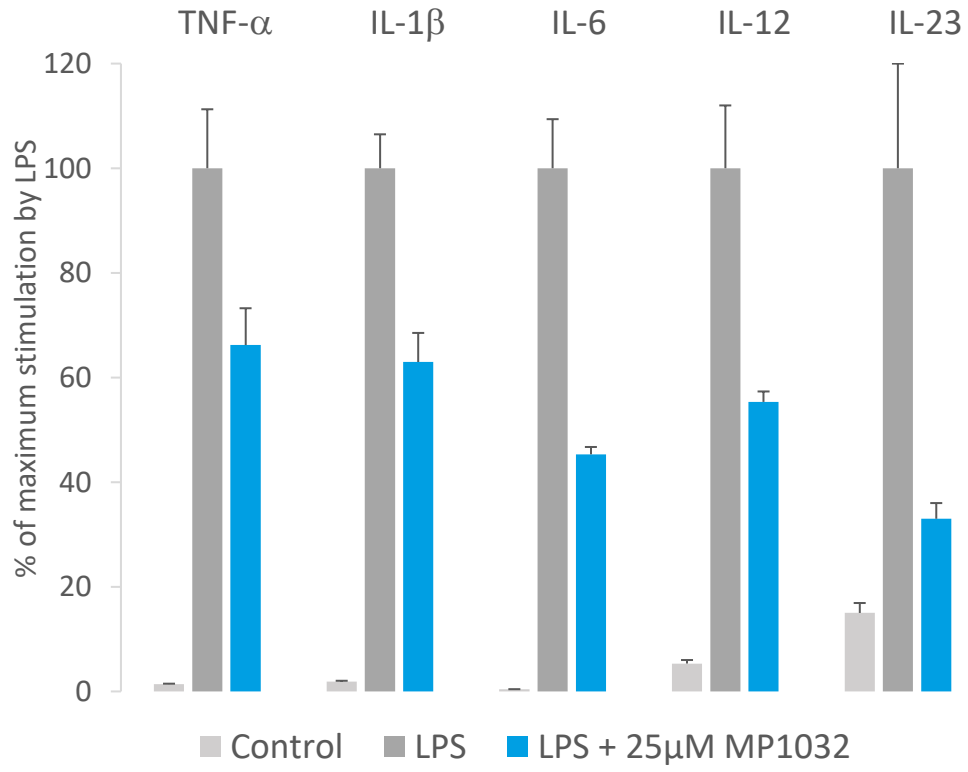
SARS (e.g. SARS-CoV-2) Influenza, RSV

The redox balance of (immune) cells is a key signaling pathway which affects energy metabolism, inflammatory pathways (NFkB, Nrf2), pathogen defense mechanisms and tumor microenvironment. Redox balance is disturbed by metabolic re-programming, which in turn drives disease pathology. MP1032 is a small-molecule metabolic modulator which re-balances cellular redox state.

MP1032 Acts Upstream of Multiple Inflammatory Pathways
Thereby Enhancing the Efficacy of Other Anti-Inflammatory Therapeutics



MP1032 down-modulates major inflammatory cytokines to physiological levels*



* in primary mouse macrophages
LPS: lipopolysaccharides

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First-In-Class Self-Regulated Molecular Mechanism of Action

MP1032 is only Activated by Elevated ROS Concentrations in Immune Cells

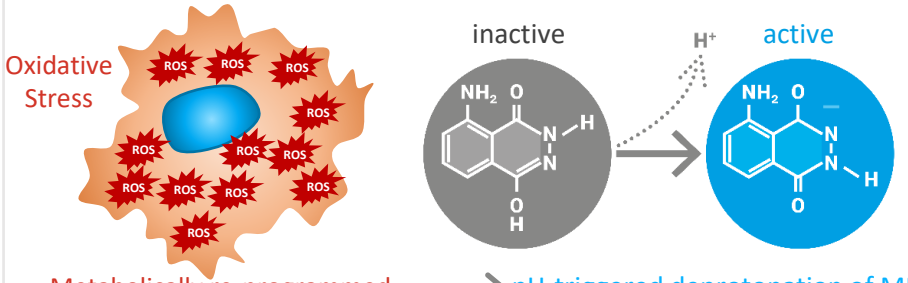
1| Physiologic State

MP1032 remains inactive at physiologic (balanced) redox state

Macrophage with physiologic mitochondrial redox balance → MP1032 **inactive**

2| Pathogenic (Re-Programmed) State

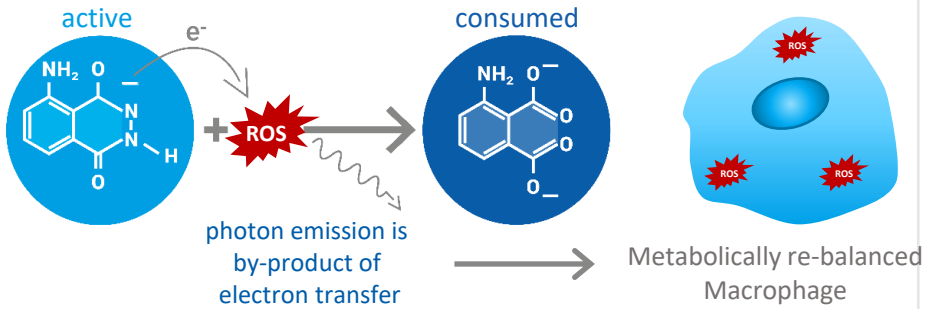
High ROS concentrations create spots of high pH, which **activates** MP1032



Metabolically re-programmed Macrophage → pH-triggered deprotonation of MP1032

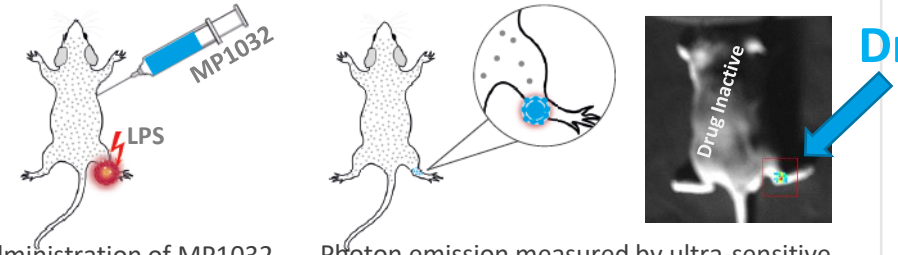
3| Balancing Redox State by Electron Transfer

MP1032 modulates cellular redox state by triggered electron transfer



4| **Targeted** Drug Activity

MP1032 in vivo detection of drug-activity-related photon emission



Systemic administration of MP1032 to animal with LPS-induced localized inflammation

Photon emission measured by ultra-sensitive photon-counting cameras shows **targeted** drug activity only in the affected joint

Due to its molecular structure, MP1032 is **only activated by elevated ROS levels (=oxidative stress) in pathologically metabolically reprogrammed cells.** MP1032 **does not interfere with the normal redox balance that is essential for physiological cell signaling and cell metabolism**. This **self-regulated activation mechanism limits** the redox modulatory effect of MP1032 **exclusively to (immune) cells under oxidative stress**. Once the cellular redox balance is restored, the **activation of additional drug molecules stops** and the **drug activity ceases**. This auto-regulatory activation mechanism ensures that the **modulatory activity of the drug stops** when physiological redox balance is achieved, **without overshooting into reductive stress**.

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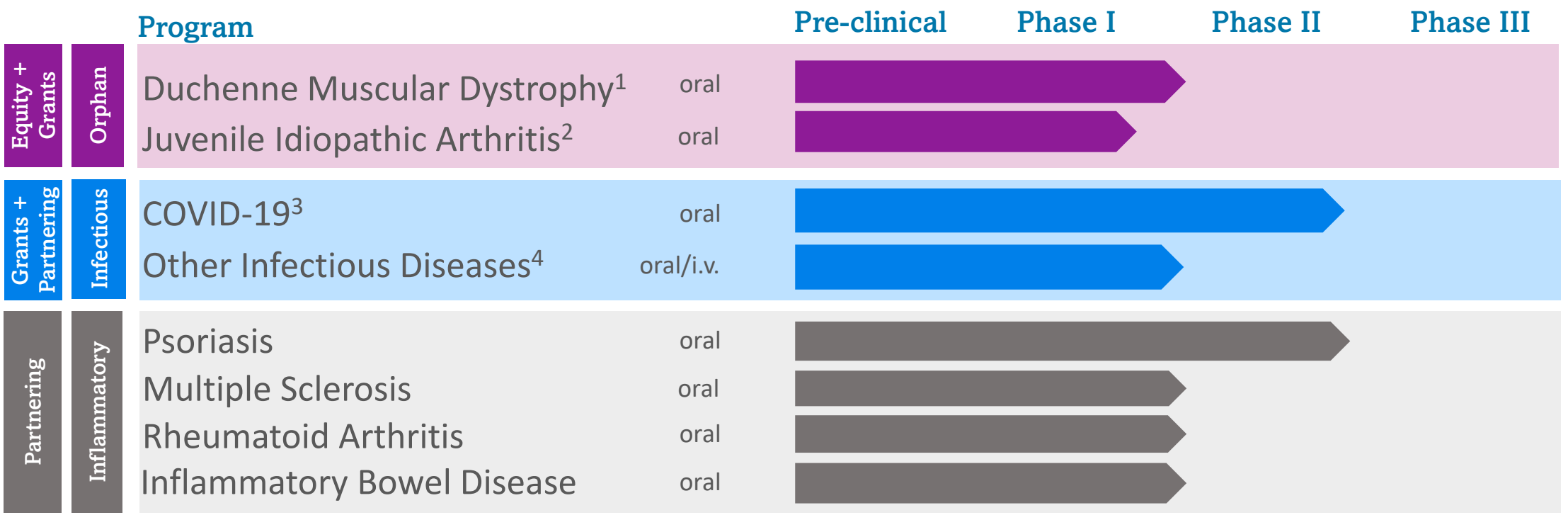
MP1032 Pipeline – Initial Focus on Orphan Diseases



[1] Recently received **Orphan Drug Designation** and **Rare Pediatric Disease Designation from FDA** in 2023; further orphan muscular dystrophy indications such as e.g. **Becker's Muscular Dystrophy** with similar standard anti-inflammatory therapy

[2] On the basis of preclinical in vivo studies for Rheumatoid Arthritis

[3] Phase IIa financed by **EU grant of EUR7.9m**; data were published in ***Lancet Regional Health (Europe);*** this study could serve as PoC for **Host-Directed** Therapies for potentially pandemic infectious diseases such as **COVID, RSV, Influenza** ("**Pandemic Preparedness**")

[4] E.g. **Sepsis,** Multi Drug Resistant Infections, *Clostridioides difficile*, Acute Respiratory Distress Syndrome (ARDS)

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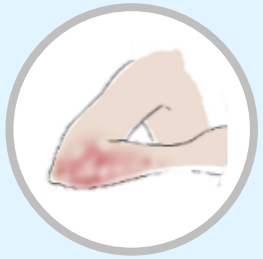
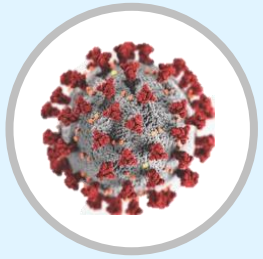
Proven Efficacy and Safety

Efficacy and safety studies conducted with MP1032 as stand-alone drug (monotherapy)



Efficacy ✓
Safety ✓

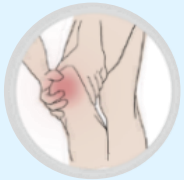
Psoriasis



Efficacy ✓
Safety ✓

COVID-19

- Outstanding safety demonstrated in over 234 patients treated with MP1032 in 4 double-blind placebo-controlled clinical trials.
- Anti-inflammatory and disease-modifying effect demonstrated in two Phase II trials in psoriasis.
- Anti-inflammatory and anti-infective effect shown in a recent Phase II study in COVID-19 patients



Rheumatic Diseases

Crohn's U. Colitis

Multiple Sclerosis

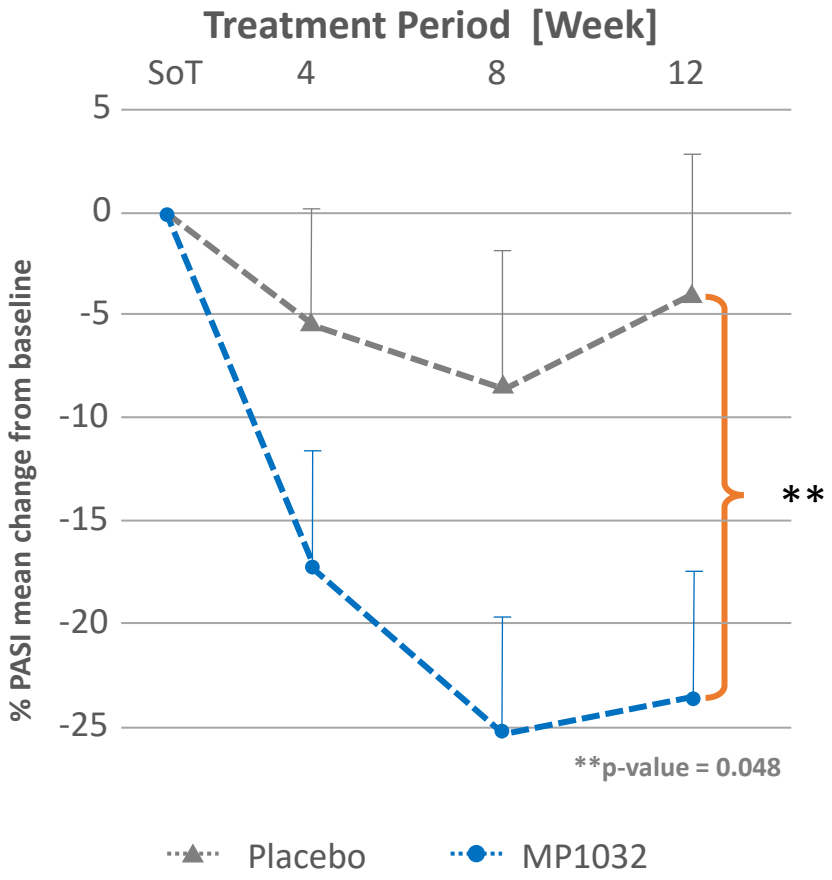
Duchenne Muscular Dystrophy

- Efficacy and therapeutic effectiveness demonstrated in pre-clinical (animal) models of common chronic inflammatory diseases and in animal model of the orphan childhood disease Duchenne Muscular Dystrophy.

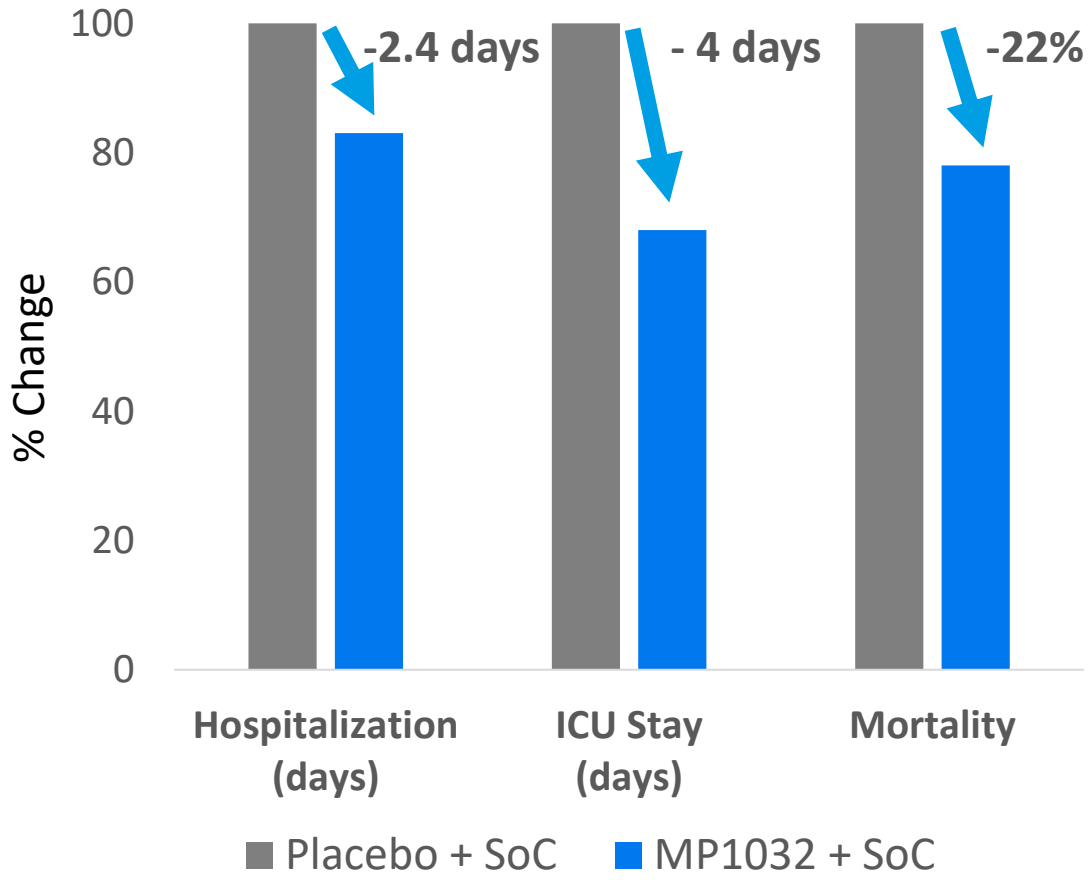
Clinical Data

3 Completed Phase II PoC Studies Demonstrated Disease-Modifying Efficacy and Outstanding Safety

Plaque Psoriasis (PASI 10-15) Phase IIa



Moderate-to-Severe COVID-19 Phase IIa*



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*Data were published in February 2024 in **Lancet Regional Health - Europe**

MP1032 Safety

Outstanding Safety Profile Pre-Clinically and in Humans

Pre-clinical

Max. oral dosing
6 months –
120x human dose
No dose-limiting toxicity could be reached

Max. oral dosing
12 months
30 x human dose
No observed adverse effect

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

Oral
MP1032

MP1032 demonstrated excellent safety based on data from preclinical studies and four clinical trials with 366 patients (= **234 verum** + 132 placebo).

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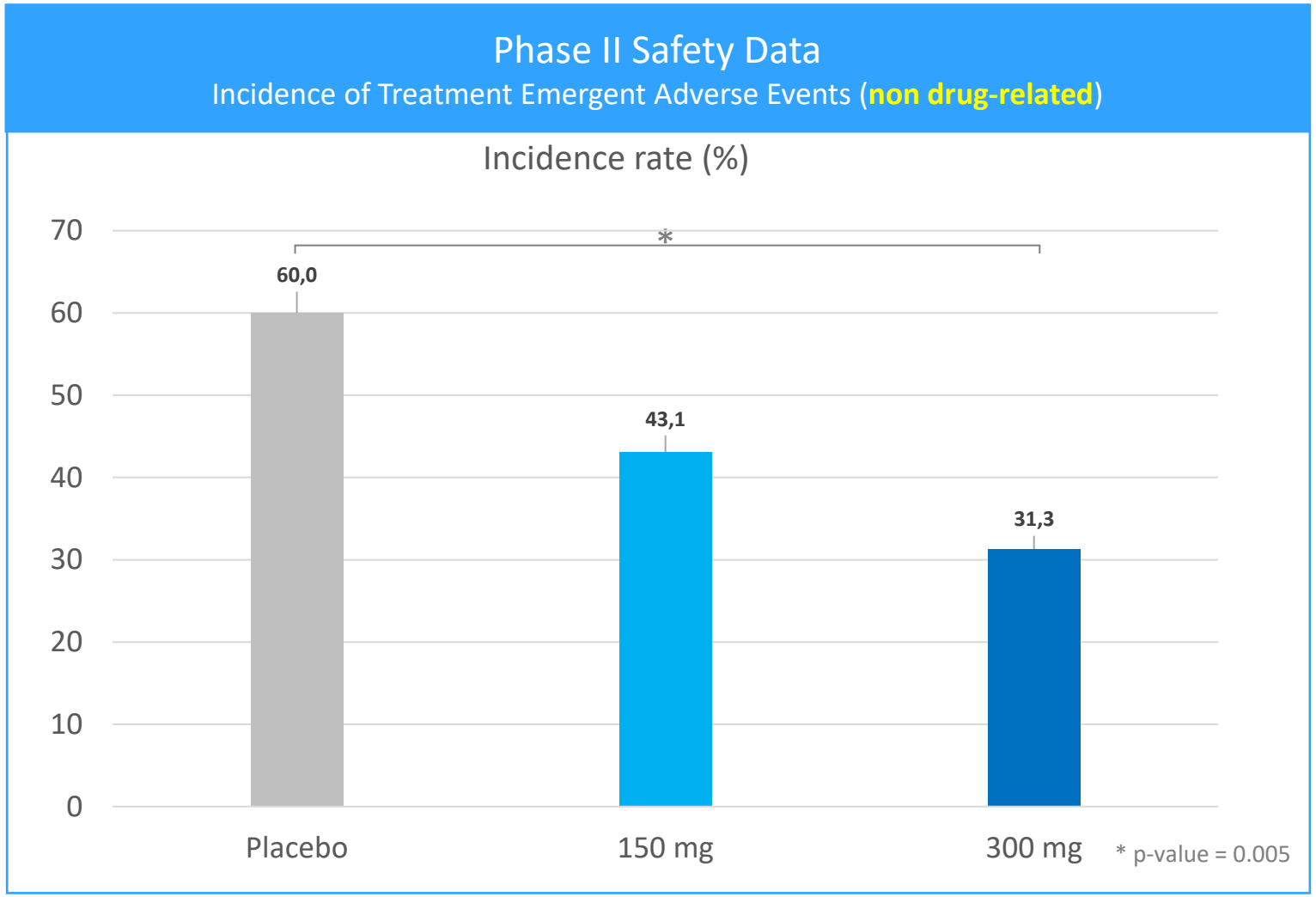
MP1032: Less TEAEs in Treatment Groups than in Placebo Group

Potential to Reduce Non-Drug-Related Adverse-Events in Fixed-Dose Combinations (FDCs)



Safety data from Phase II clinical trial MP1032-CT04 Plaque Psoriasis

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

150mg and 300 mg doses *reduce* TEAEs

SAE = Serious Adverse Event

TEAE = Treatment Emergent Adverse Events

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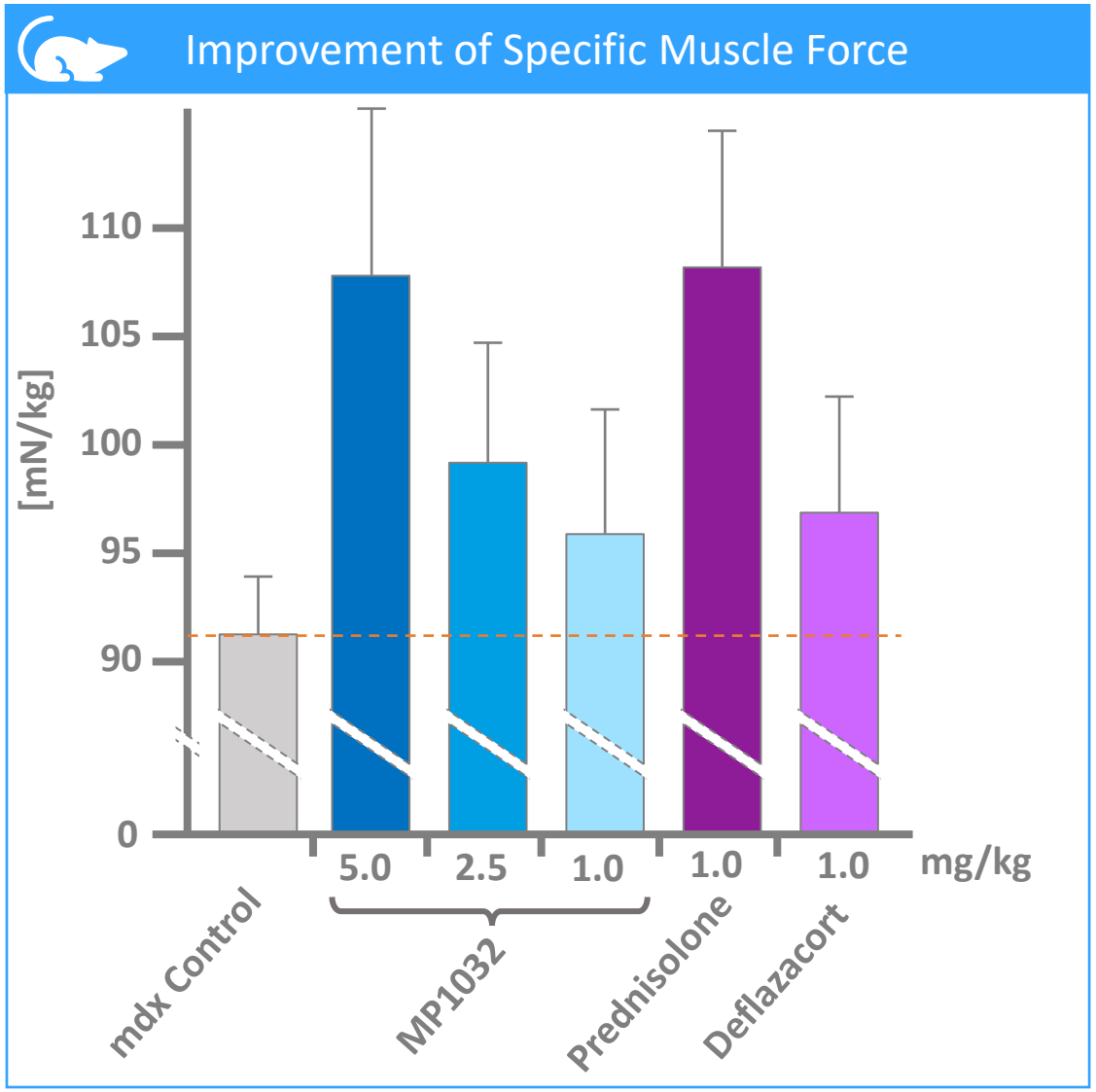
MP1032 Muscle Force Preservation Equal or Better Than Corticosteroids

in DMD Animal Model (mdx mice)



MP1032 improves EDL* muscle force from DMD *mdx* mice with same potency as corticosteroids…

(without any side effects as demonstrated in clinical phase I and II studies)

* EDL = extensor digitorum longus

Study performed by Agada Research Ltd. Halifax, Canada

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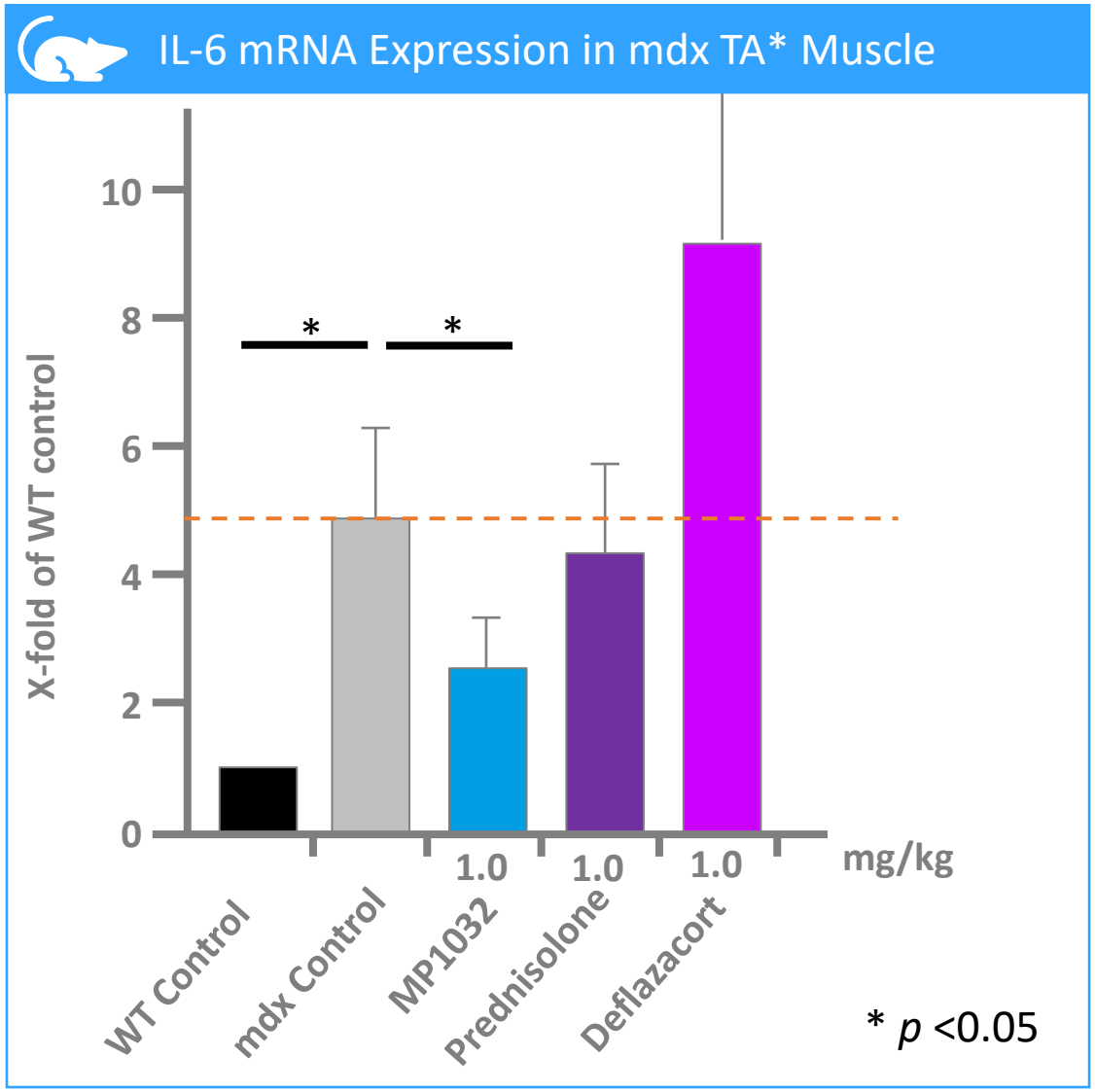
MP1032 – IL-6 Inhibition in Muscle by MP1032 is Better than by Corticosteroids

in DMD Animal Model (mdx mice)



MP1032 elicits meaningful inhibition of IL-6 in TA* muscle of *mdx* mice.

This cytokine inhibitory effect was also seen for IL-1β, TNF-α and CD163 and underlines the efficacy of MP1032 in treatment of DMD.

* TA = Tibialis Anterior

Study performed by Agada Research Ltd. Halifax, Canada

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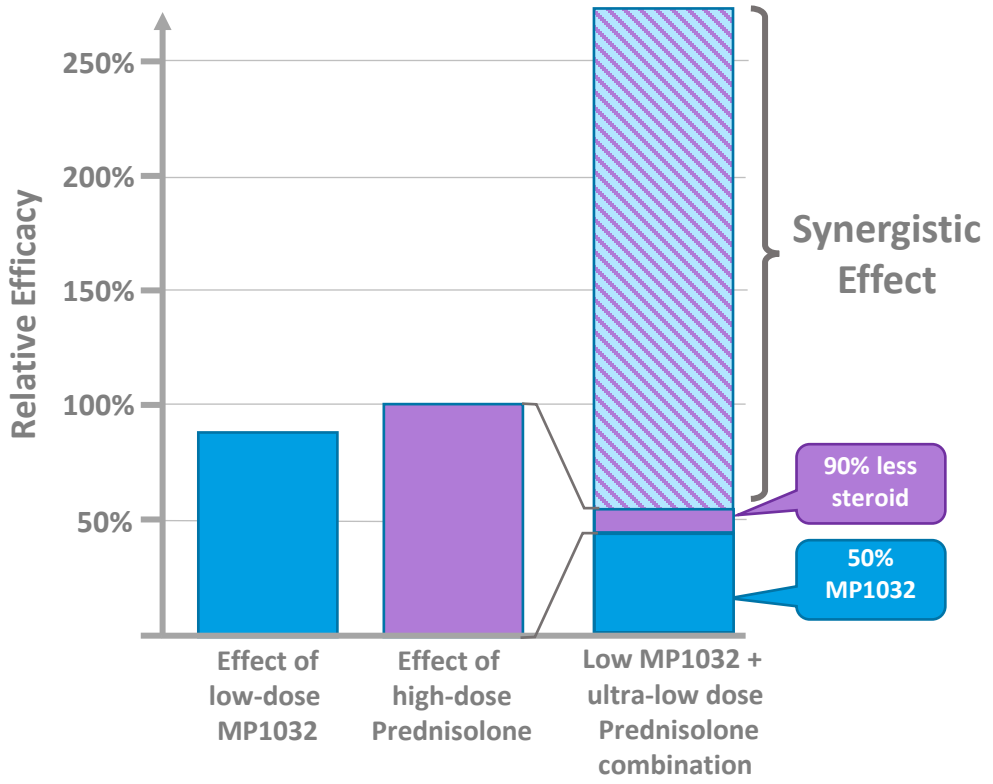
MP1032 Boosts Corticosteroid Anti-Inflammatory Potency

Efficacy ⇈ Side-effects ⇊

Cumulative Synergistic Effect on Cytokine Panel



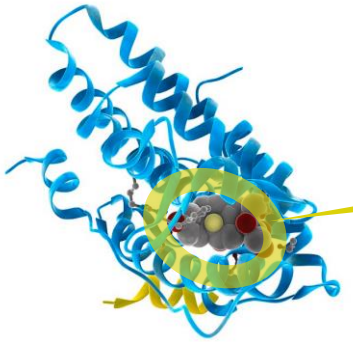
BioMap Assay performed by Eurofins

Oncology

Oncology 2000;59(suppl 1):13–18

Redox Regulation of the Nuclear Receptor

Hirotoshi Tanaka[a] Yuichi Makino[b] Kensaku Okamoto[b] Takahisa Iida[b] Noritada Yoshikawa[b] Takanori Miura[b]



Redox-sensitive region (Cys 481) in vicinity of GCR Ligand Binding Domain

The **synergistic effect** seems to be due to the **glucocorticoid receptor's cysteine-rich ligand binding domain**, which is **sensitive to changes caused by redox changes**/oxidative stress/ROS. This weakens steroid binding in cells under oxidative stress, **necessitating higher steroid doses for the same effect. MP1032 can reverse these changes** and **restores optimal steroid binding**. Thus, **MP1032 enables lower doses of glucocorticoids**.

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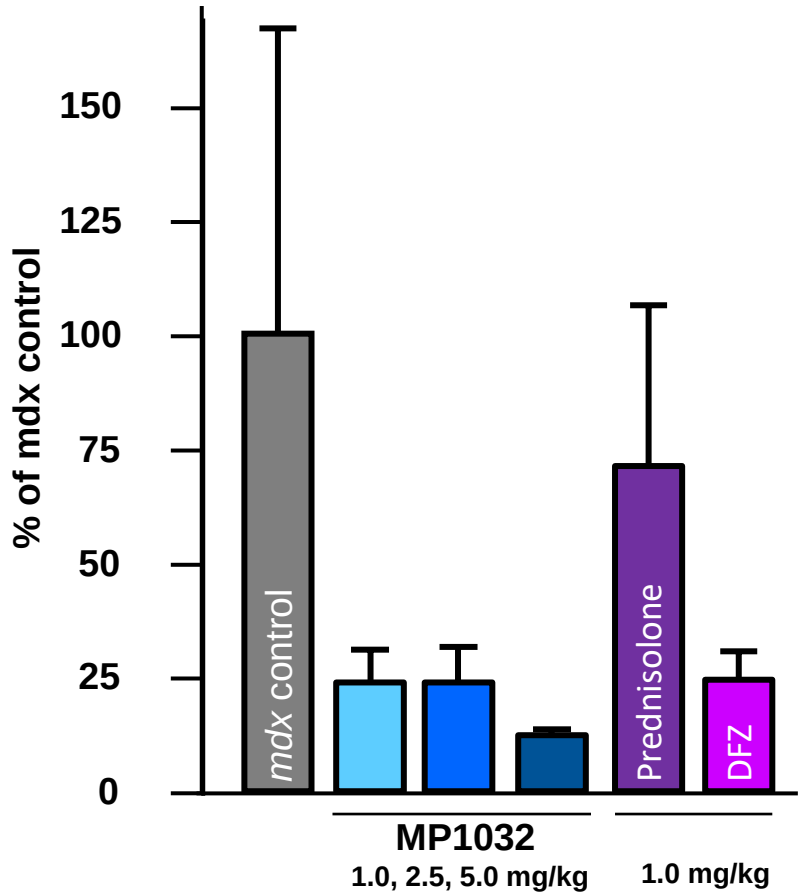
MP1032 Has Stronger Anti-Inflammatory Effects Than Corticosteroids

in DMD Animal Model (mdx mice)

Histological Inflammation in Muscles



Less inflammatory foci in muscles

mdx mice treated with MP1032 showed less histological inflammatory foci in TA* muscle than *mdx* mice treated with Prednisolone or Deflazacort.

* TA = Tibialis Anterior

Study performed by Agada Research Ltd., Halifax, Canada

MP1032 and DMD: Summary of Experimental Data and Rationale

Experimental data with MP1032

- Reduces pro-inflammatory cytokines like IL-6, IL-1b and TNF-α - similar to Corticosteroids (partly better than Corticosteroids (e.g. IL-6)
- Reduces inflammatory foci in muscles of *mdx* mice (better than Corticosteroids)
- Improves *ex vivo* muscle specific force in *mdx* mice, dose dependent, similar to corticosteroid treatment
- Lacks growth-related side effects of Corticosteroids in mice
- Acts synergistically with Prednisolone and Vamolorone

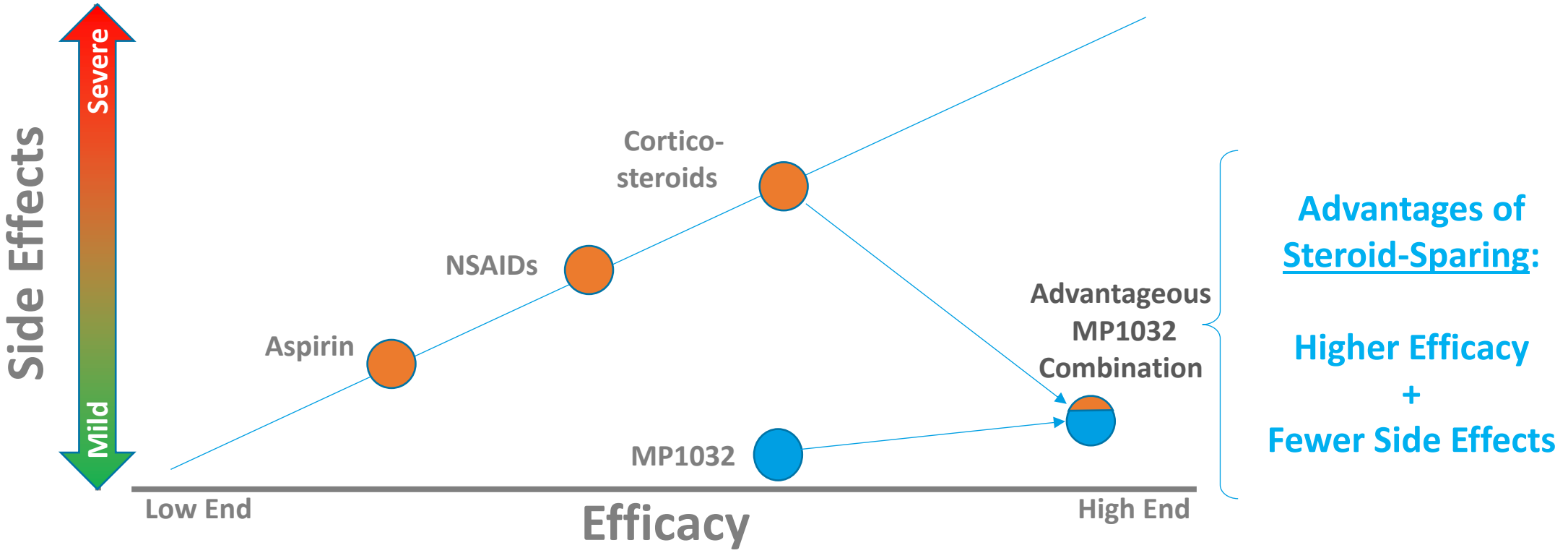
Rationale & Benefits of MP1032 as DMD therapy

- Inflammation in muscles is a major issue in DMD
  - MP1032 is anti-inflammatory
- Current therapies with long-time use of steroids (e.g. Prednisolone, Deflazacort or Vamorolone) cause serious side effects
  - MP1032 has nearly no side effects (as demonstrated in Phase I and 3 Phase II studies)
  - MP1032 synergistically enhances effects of Corticosteroids, suggesting a steroid-sparing use
- Other approved therapies e.g. like Ataluren (Translarna®) only suitable for small subset of DMD patients
  - In contrast, MP1032 not restricted to subsets of patients (upstream MoA with effects on several inflammatory pathways)

Next Steps

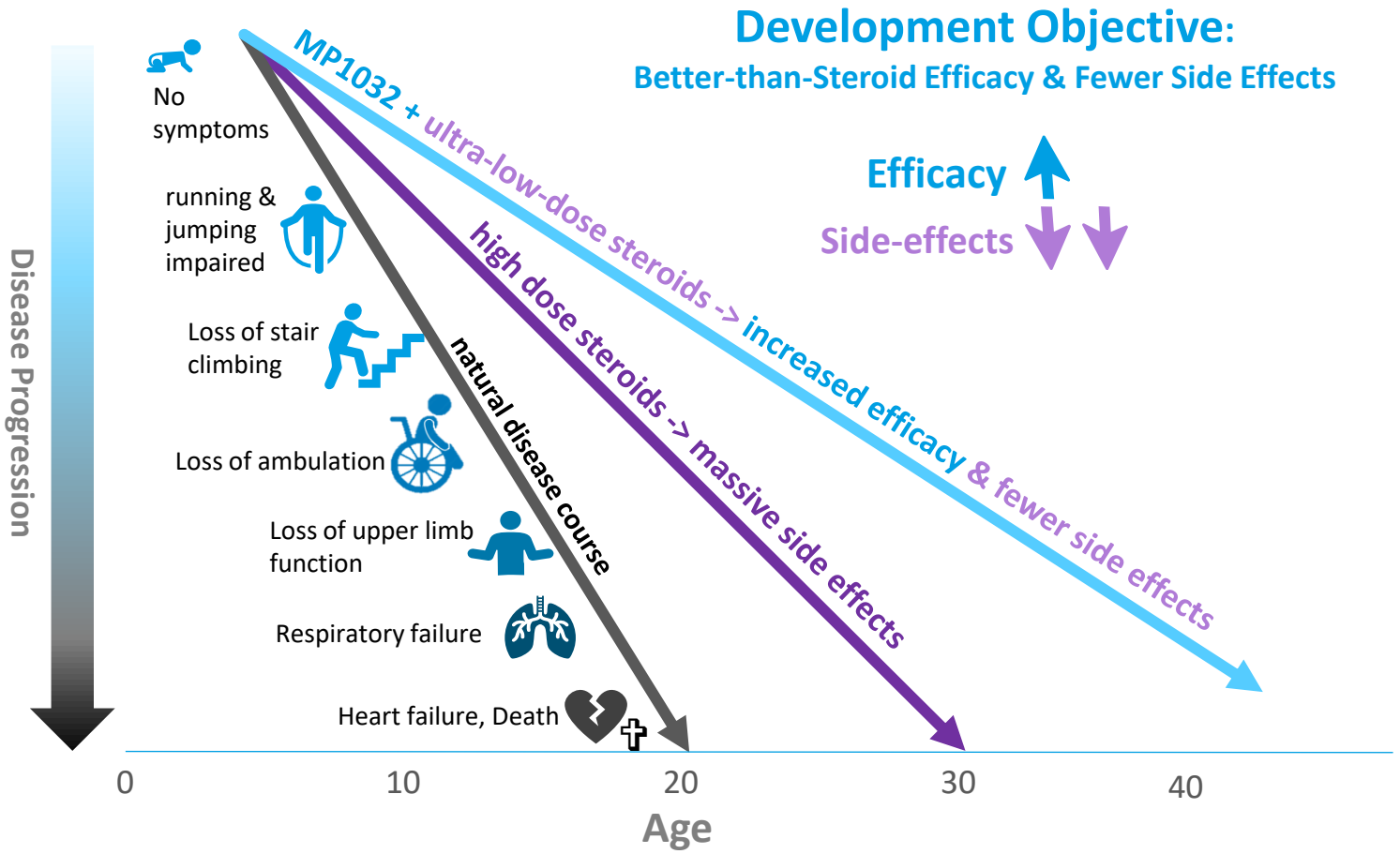
- MetrioPharm plans a Phase II clinical study, starting in 2025
- Proposals of CROs are currently investigated

Combinatorial Drug Repositioning Strategy in DMD, Rheumatoid Arthritis & further Indications with Corticosteroid Standard Therapies



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**

Duchenne Muscular Dystrophy (DMD)



Steroid side effects, e.g.

- Growth retardation
- Cushing syndrome
- Osteoporosis
- Hypertension
- Behavioral changes

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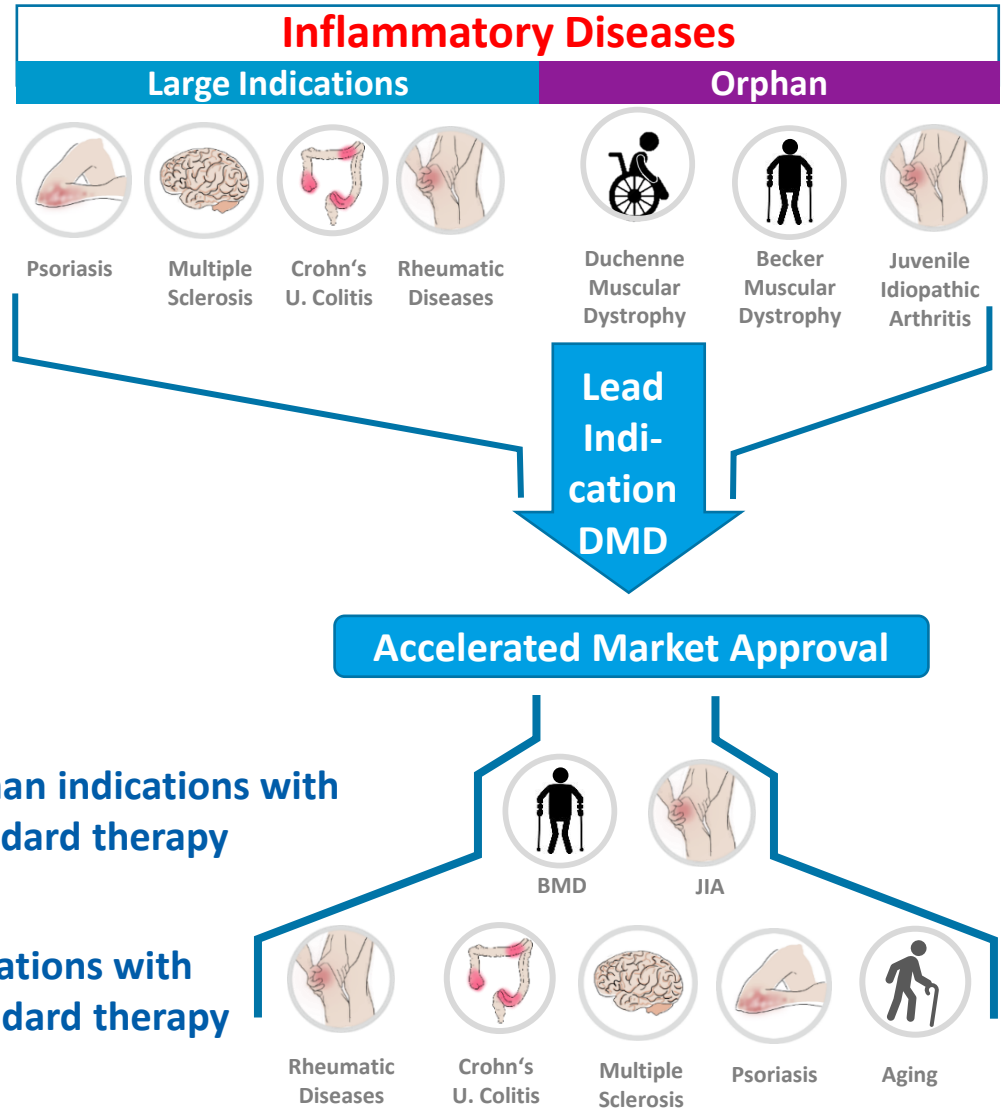
Development Strategy: Initial Focus on Orphan Diseases



Duchenne Muscular Dystrophy

- **High medical need**
- **Orphan disease**
- **Regulatory fast track**
- **Strong support from patient organizations**

Expansion into other orphan indications with similar corticosteroid standard therapy

Expansion into large indications with similar corticosteroid standard therapy

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Corticosteroid Sparing – A Significant Market Opportunity

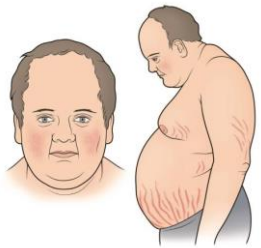
Corticosteroids: still the most widely used therapy for e.g.

Orphan Opportunities	Large Non-orphan Indications		
• **Duchenne Musc. Dystrophy** • Juvenile Idiopathic Arthritis • Becker Muscular Dystrophy • Other Muscular Dystrophys • Autoimmune Hepatitis	• **Psoriasis** • **Rheumatoid Arthritis** • **Inflammatory Bowel Disease** • **Multiple Sclerosis** • **COVID-19 (hospitalized)**	• Syst. Lupus erythematosus • Sarcoidosis • Polymyalgia Rheumatica • Polymyositis • Urticaria	• Asthma • COPD • Interstitial Lung Disease • Rhinitis • Contact Dermatitis

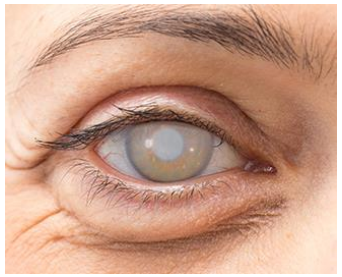
Corticosteroids: highly effective - but problematic side-effect profile

Heart Damage

Osteoporosis



Cushing Syndrome



Eye Damage

Growth Retardation

+ Further Side Effects

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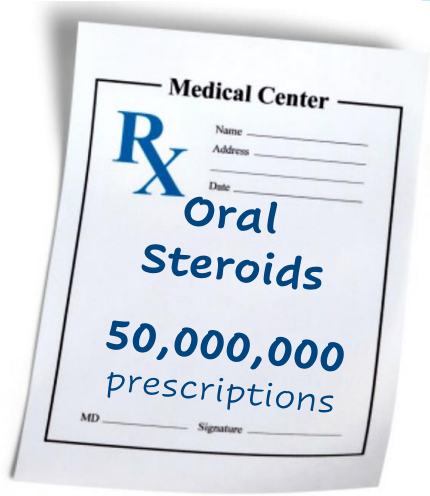
Glucocorticoid Market Opportunity

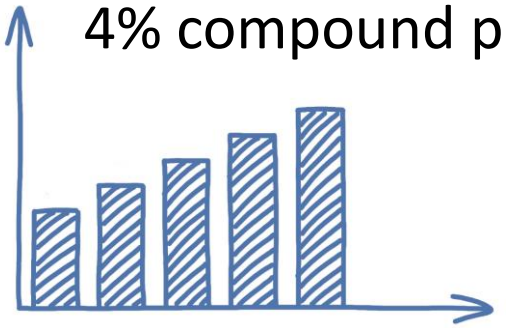


5 Big EU

Total Addressable Market: Worldwide Estimated >>200 Million Prescriptions per Year

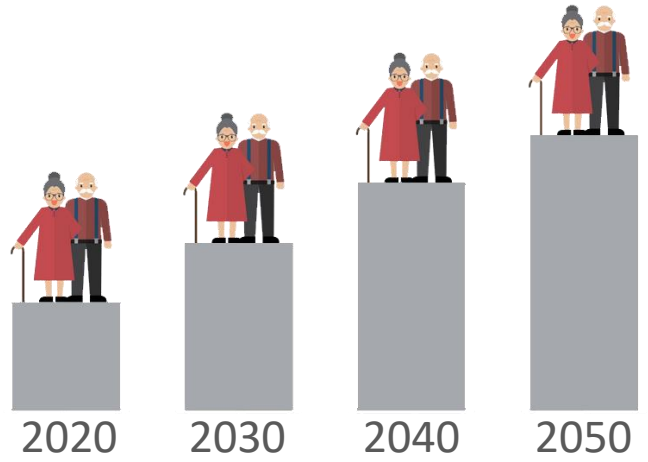
Projected Market Growth

4% compound per year



Growth Drivers:

- Aging
- Demographic Change
- Rise in Chronic Diseases



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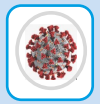
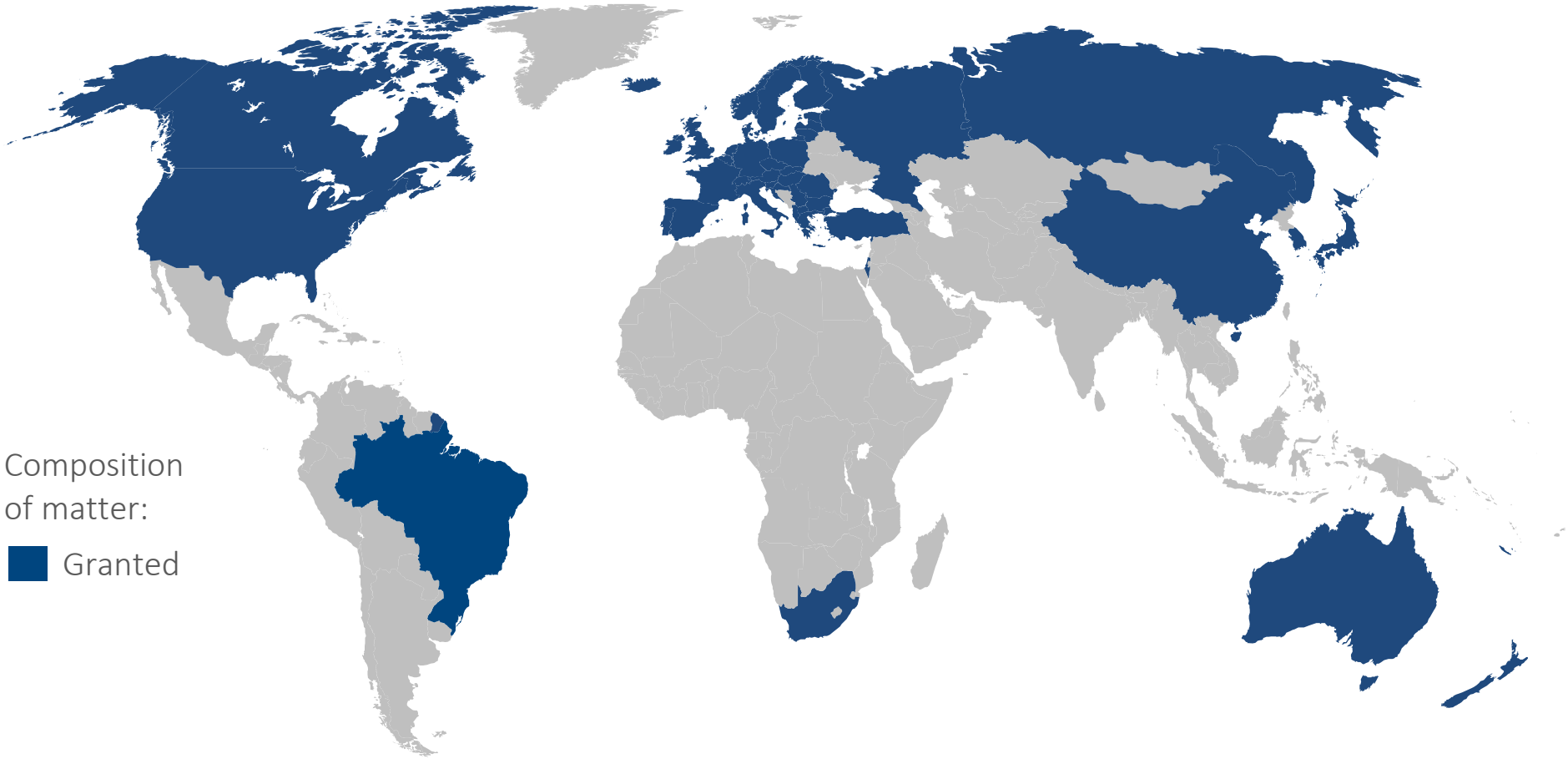
Total Market Size for MetrioPharm Pipeline

Indication	Medical Need & Market Opportunity	Total Market Size
 **Duchenne Muscular Dystrophy**	Steroid-sparing therapies with improved disease-slowing properties and outstanding safety profile (PoC for other inflammatory diseases)	**$ 4 Billion**
 **Juvenile Idiopathic Arthritis**	Steroid-sparing therapies with improved disease-slowing properties and outstanding safety profile (PoC for other inflammatory diseases, see below)	**$ 2 Billion**
 **Psoriasis**	A safer and more effective oral drug, especially for the large, underserved segment of mild-to-moderate psoriasis (e.g. by steroid-sparing)	**$ 26 Billion**
 **Multiple Sclerosis**	A more effective oral therapy with better tolerability compared to currently leading drugs (e.g. by steroid-sparing or other fixed-dose combinations)	**$ 24 Billion**
 **Inflammatory Bowel Disease**	Oral maintenance therapies with higher response rates than salicylates and better long-term safety than corticosteroids (by steroid-sparing)	**$ 20 Billion**
 **Rheumatoid Arthritis**	An effective, oral early-intervention treatment for safe long-term use (e.g. by steroid-sparing)	**$ 28 Billion**
 **COVID-19/Long COVID & other pandemic infectious diseases**	1. **Virus-variant-independent** oral drug for safe **prophylactic & early intervention use** in **immune-compromised patients** & **Long/Post COVID** 2. PoC for host-directed therapies for other (potentially pandemic) infectious diseases such as **Influenza Virus, Respiratory Syncytial Virus** & others (see below)	**$?? Billion**
 **Other Infectious Diseases**	Host-directed therapy for **Sepsis,** Multi Drug Resistant Infections, Clostridioides difficile, Acute Respiratory Distress Syndrome (ARDS) etc.	**$ 10+ Billion**

Strong Intellectual Property Portfolio



- Strong intellectual property portfolio with 21 patent families including 98 granted patents to-date
- Composition of matter patents: valid until 2031 (plus PTE/SPC options)
- Medical use patent applications in various fixed-dose combinations: valid until **2042/2043**

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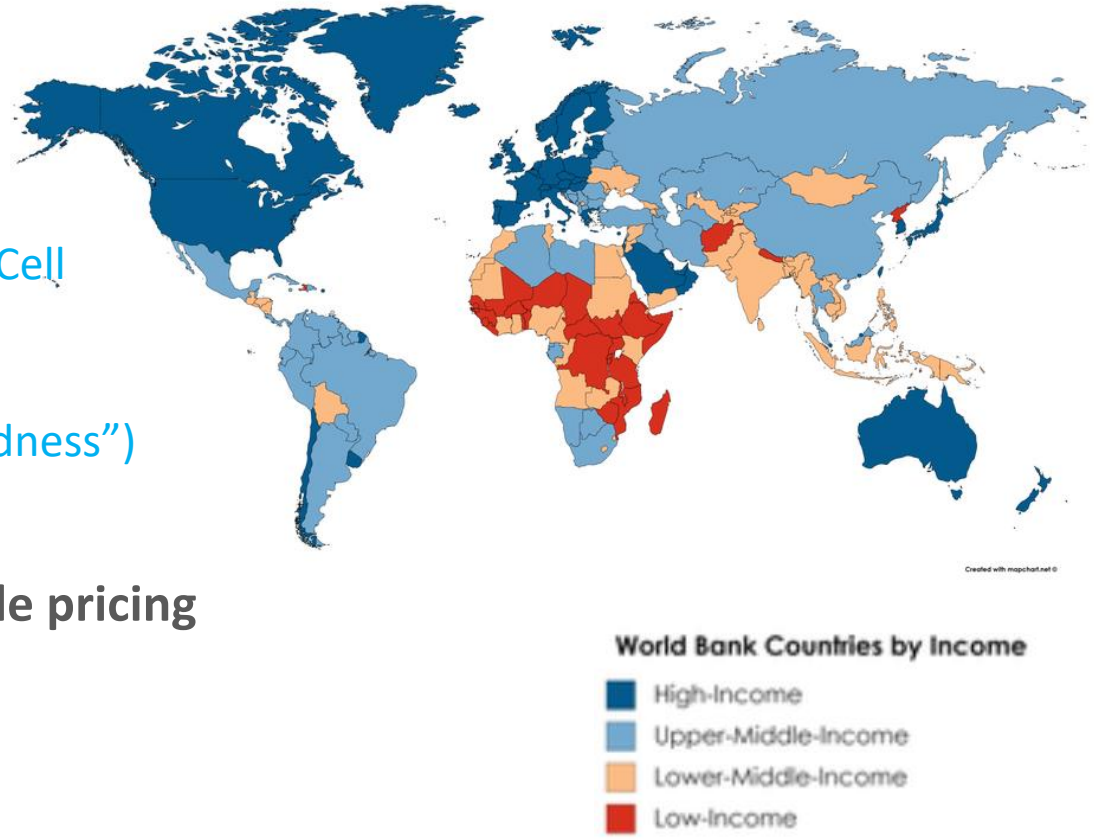
Investment with Social Impact

- **Addresses high medical needs in Low & Middle-Income Countries (L&MICs)**
  - Chronic diseases
    - Affordable alternative to high-end therapies (Biologics, Cell Therapies) which are out of reach for L&MICs
  - Infectious diseases
    - Early response to new viral threats (“Pandemic Preparedness”)
    - Anti-microbial resistance
- **Low Cost-of-Goods (manufacturing) allows for affordable pricing**
- **Ease of use in compromised environments**
  - oral
  - no cooling required
  - highly stable
- **Outstanding safety – no need for expensive patient monitoring**



Summary (1)
Platform of Oral Modulators Targeting the Mitochondrial Metabolism in Macrophages

- **First-in-class self-regulating modulators of mitochondrial metabolism in macrophages**
  - MP1032 **reverses** the **pathologically altered ("reprogrammed") mitochondrial redox balance in macrophages** back to normal
  - By down-regulating **pathologically elevated levels of ROS** (Reactive Oxygen Species) back to **physiological (normal) levels**
  - **Without (!) interfering with physiological levels of ROS,** which are essential for cell signaling & other functions of immune cells
  - Through a **first-in-class self-regulating mechanism of action** that is **activated only** when ROS levels are **elevated (pro-drug)**
  - **Activation** is initiated **through clusters of high pH levels** that trigger **deprotonation** of MP1032 which then degrades ROS
  - Once the cellular **redox balance is restored** to **physiological ROS levels**, the **activation** of further MP1032 molecules **stops**
  - Consequently, the **drug activity ceases**, i.e. MP1032 is completely **inactive at physiological (normal) ROS levels**

- **Broad anti-inflammatory activity without immune suppression**
  - MP1032 acts **upstream** of **multiple inflammatory pathways (cytokines, kinases, mitochondrial dysfunctions, senescent cells)**
  - For example, **cytokines are broadly downregulated to physiological levels - but not below physiological levels**
  - MP1032 shows **strong anti-inflammatory activity similar to corticosteroids** - but **without serious side effects**
  - MP1032 **synergistically enhances the efficacy** of other anti-inflammatory therapeutics, e.g. **corticosteroids**, **DMF (Tecfidera®)**

Summary (2)
Platform of Oral Modulators Targeting the Mitochondrial Metabolism in Macrophages

- **Host-directed antiviral and antibacterial activity**
  - -> Broad **host-directed** & **dose-dependent antiviral activity** against **6 tested variants of COVID**
  - -> **Host-directed antiviral activity also** against other **RNA-based viruses** (e.g. **RSV, Influenza)**
  - -> Strong **host-directed antibacterial activity** against **several tested bacterial strains including multidrug-resistant strains**
  - -> **Host-directed therapy** is a promising approach for treating **antibiotic-resistant bacterial strains**

- **Excellent safety profile** - especially **no immunosuppression**
  - -> **Dose-limiting toxicity could not be reached –** even though up to **1,000 times the human dose** has been administered
  - -> **Not a single drug-related serious adverse event** was observed in **4 clinical** trials with **366 patients** (**234 verum** + 132 placebo)
  - -> **Fewer treatment-emerging adverse events** (non-drug related) in the **treatment groups versus placebo** (dose-dependent!)

- **Strong intellectual property portfolio**
  - -> **21 patent families** including **98 granted patents**
  - -> Additional **medical use patents pending valid until 2042/2043**

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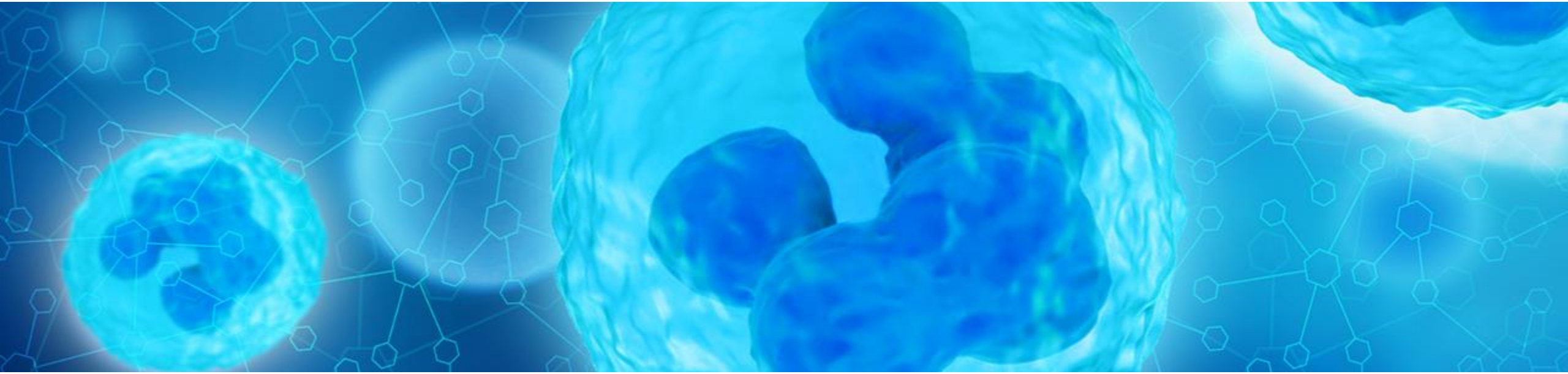
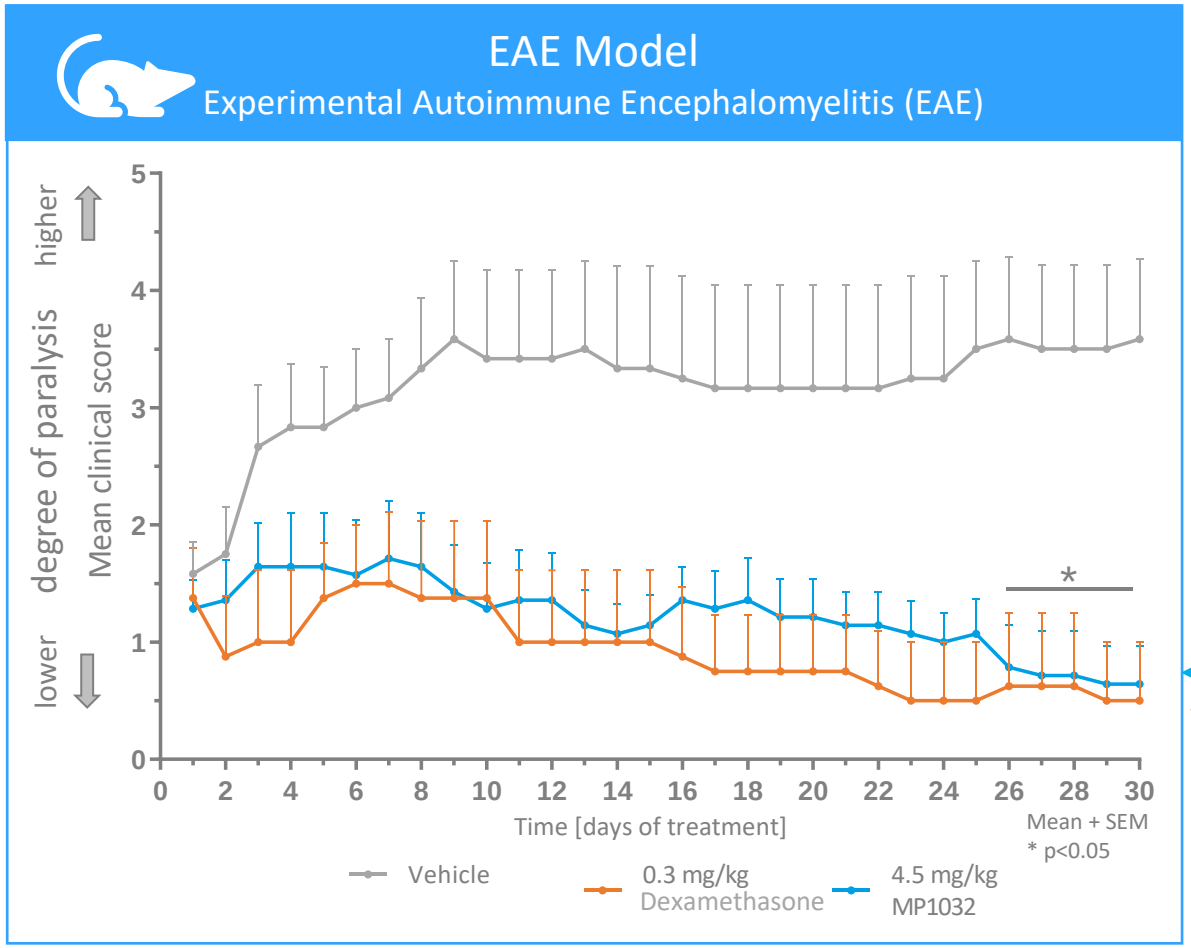


APPENDIX

Selection of Efficacy Studies in Inflammatory and Infectious Diseases

Pre-Clinical : Multiple Sclerosis EAE Model

Multiple Sclerosis



Placebo = Paralysis

MP1032 = No Disease Progression

Dexamethasone (corticosteroid)

Study conducted by Prof. Nicoletti, University of Catania, Italy

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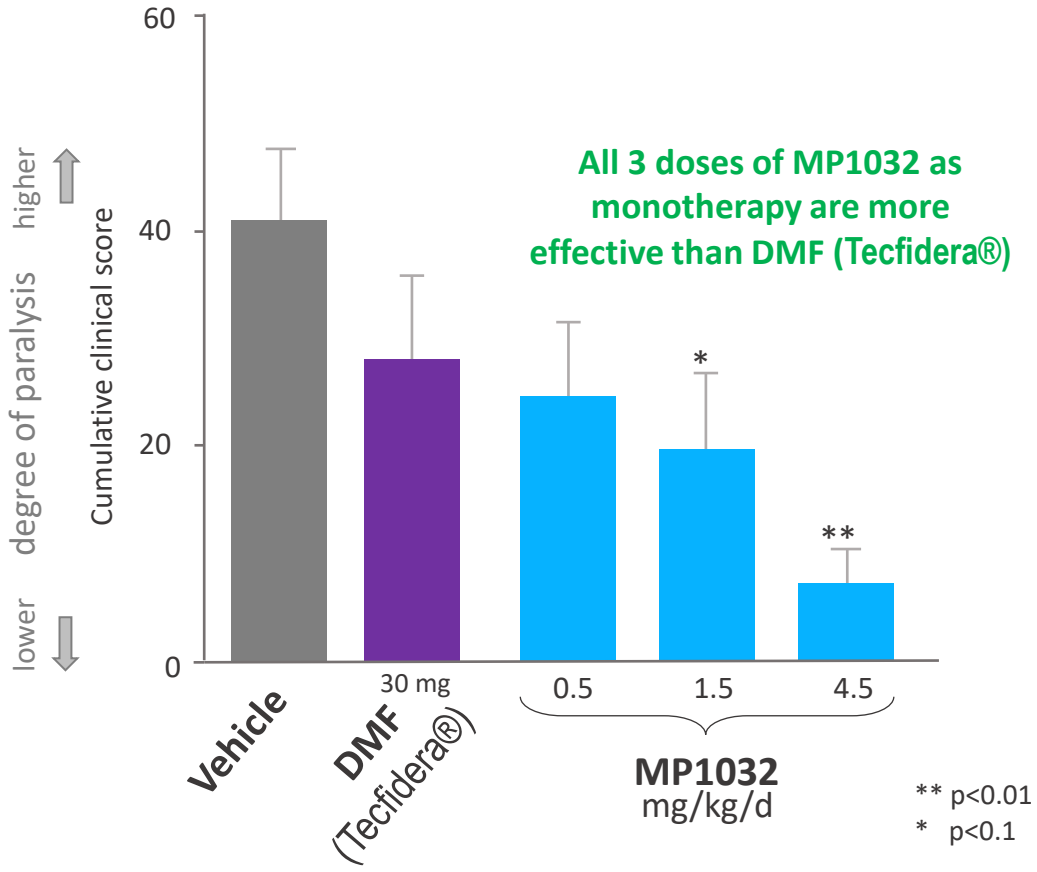
MP1032 works better than leading oral MS drug

MS

EAE model

MP1032 comparison to leading standard of care: DMF

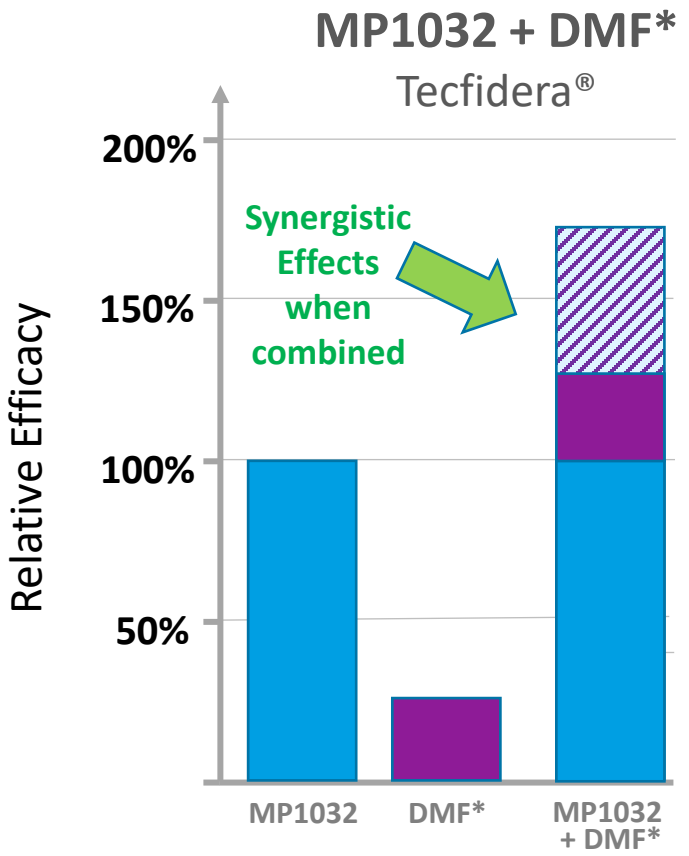


Study conducted by Prof. Nicoletti, University of Catania, Italy

Synergism with Best-in-Class Potential for MS

Cumulative Inhibition of Cytokines

IL-6 IL17a/f TNF-α



BioMap Assay performed by Eurofins

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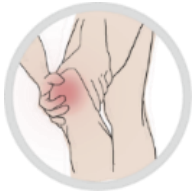


Rheumatoid Arthritis

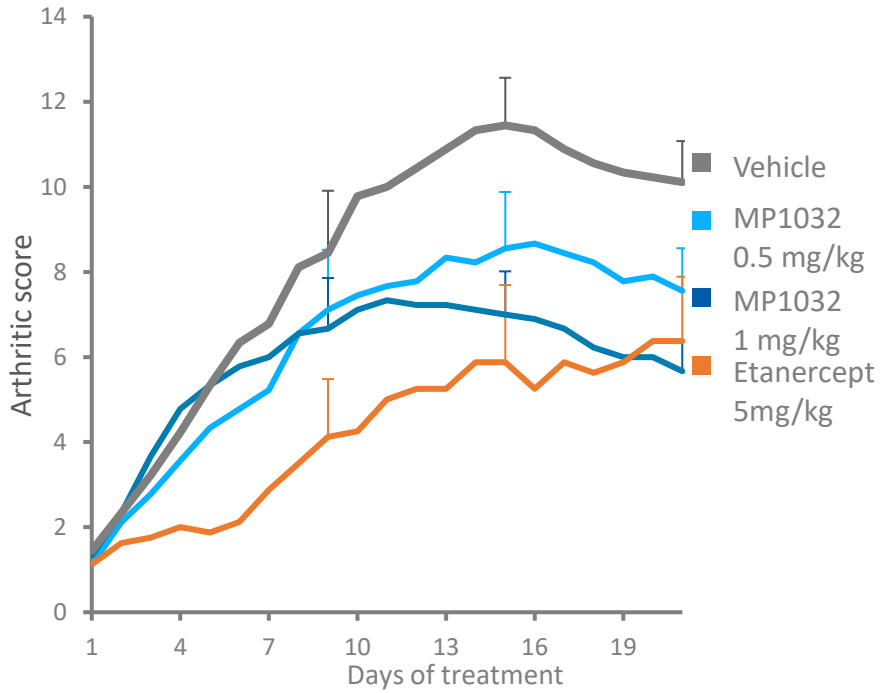
Pre-Clinical POC: Rheumatoid Arthritis (1)

MP1032 improves Arthritic Disease Score and Joint Preservation in CIA Model

Collagen-Induced Arthritis (CIA) mouse model

Improvement of arthritic score

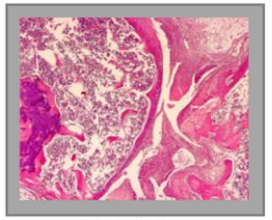
- lower is better -



In Collagen-induced arthritis (CIA) mouse model, MP1032 treatment resulted in significantly improved arthritic disease score, **on par with TNF-inhibitor Etanercept (Enbrel®).**

Knee Joint Histology Cross-sections (day 20)

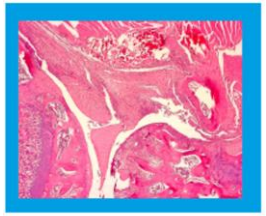
Placebo



Vehicle

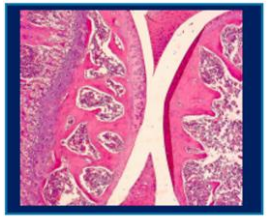
Cross section of hind-leg knee joint, showing massive infiltration and destruction of jont morphology

MP1032



0.5 mg/kg

Low-dose MP1032 results in less infiltration and partial joint preservation.



1.0 mg/kg

High-dose MP1032 results in minor infiltration and complete joint preservation.

Histological assessment showed dose-dependent disease modifying effect in form of joint preservation.

Studies performed by Prof. Nicoletti, University of Catania, Italy

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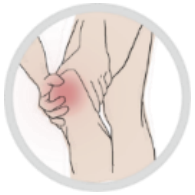


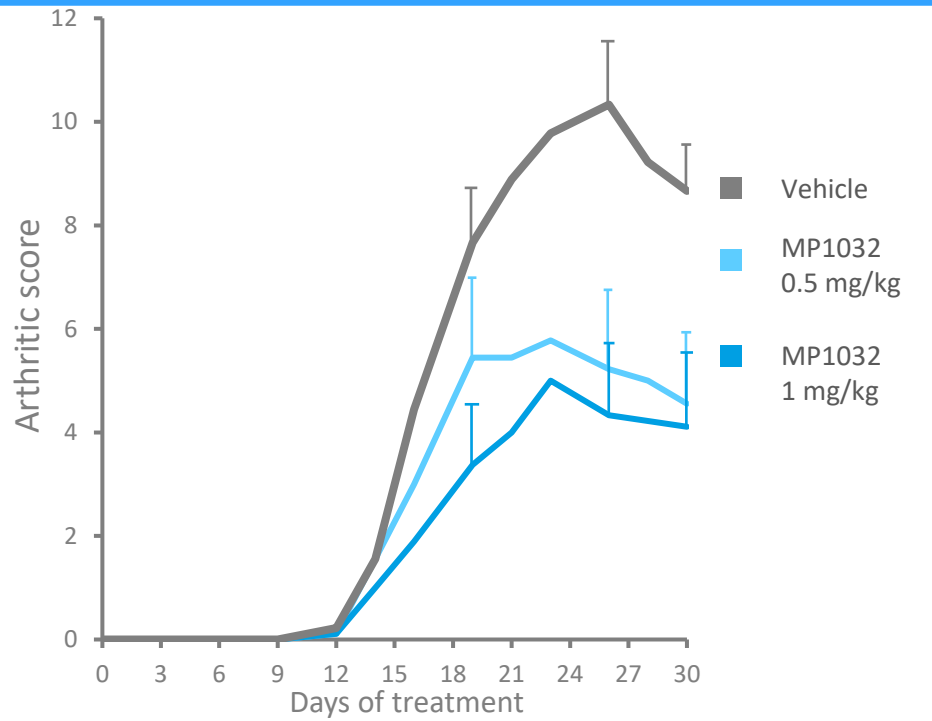
Rheumatoid Arthritis

Pre-Clinical: Rheumatoid Arthritis Model (2)

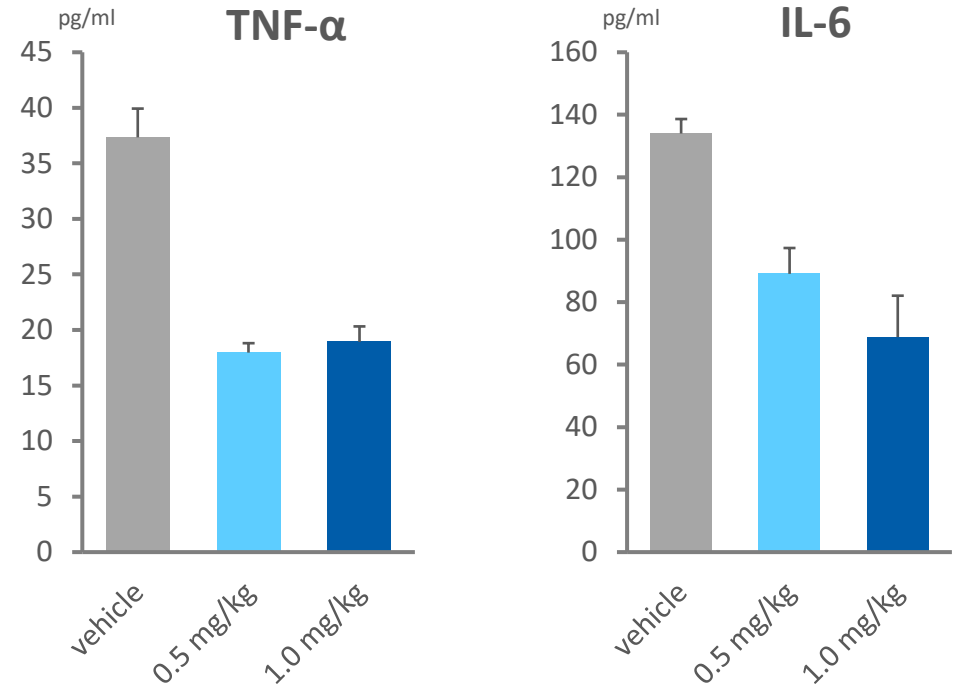
Antigen-Induced Arthritis (AIA) mouse model

Improvement of Arthritic Score

- lower is better -



Cytokine Inhibition (day 23)



In this antigen-induced arthritis (AIA) mouse model, MP1032-mediated immune metabolic modulation improved arthritic disease score compared to vehicle.

MP1032 induced a significant inhibition of two key pro-inflammatory cytokines involved in auto-immune arthritis in mouse AIA model.

Studies performed by Prof. Nicoletti, University of Catania, Italy

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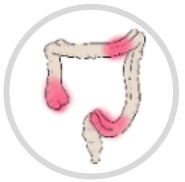


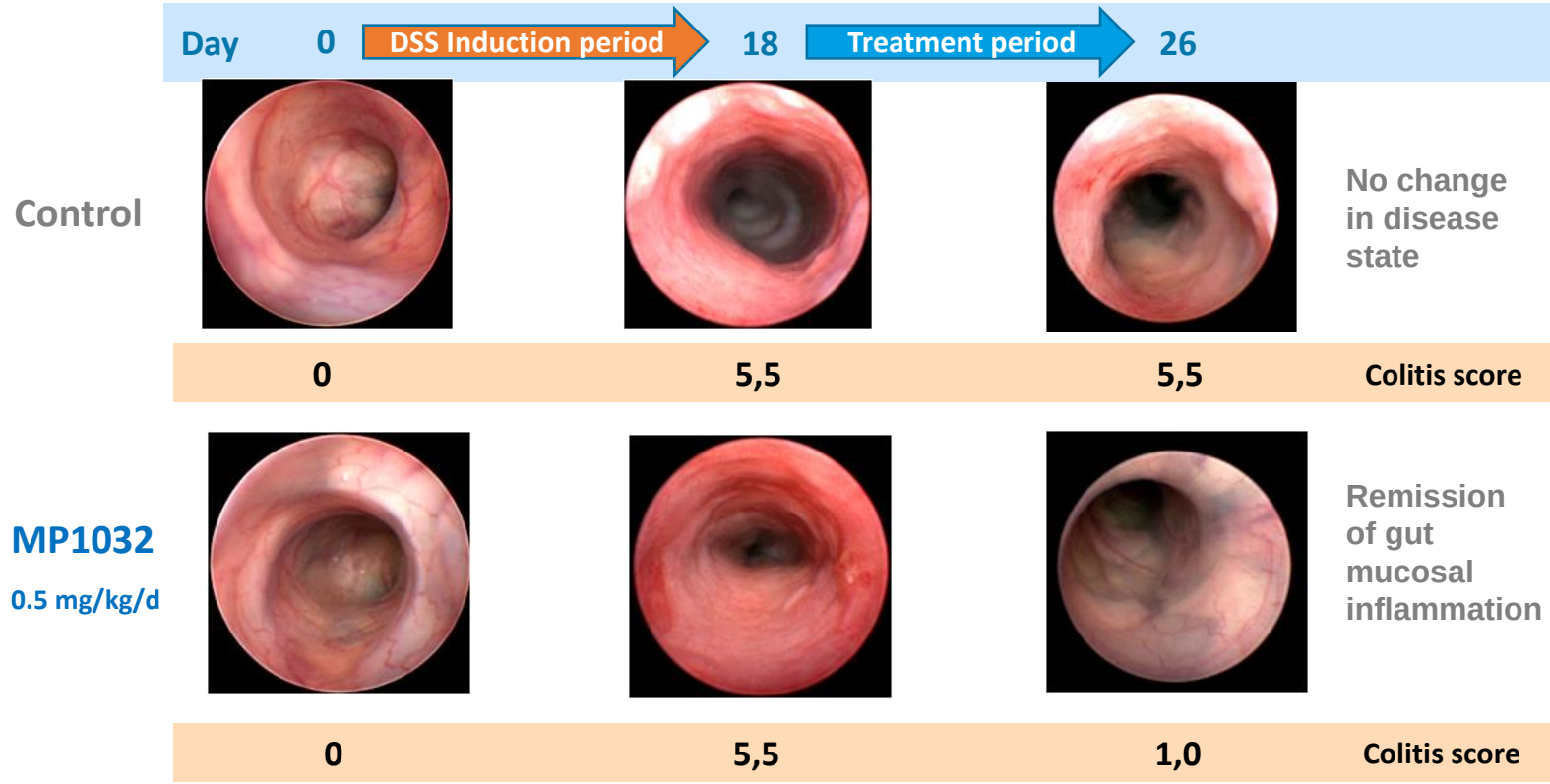
Crohn's
U. Colitis

Pre-clinical POC: Inflammatory Bowel Disease

MP1032-mediated metabolic modulation improves gut inflammation in DSS-induced Colitis Mouse Model

DSS-induced Colitis MouseModel

Endoscopic images from colon



In DSS-induced colitis mouse model. Systemic once-daily treatment with MP1032 metabolic modulator after full induction (therapeutic treatment) resulted in a near-complete remission of gut mucosa within 8 days. Endoscopic images of colon.

Study perfomed by Dr. Grötzinger, Charité, Berlin, Germany

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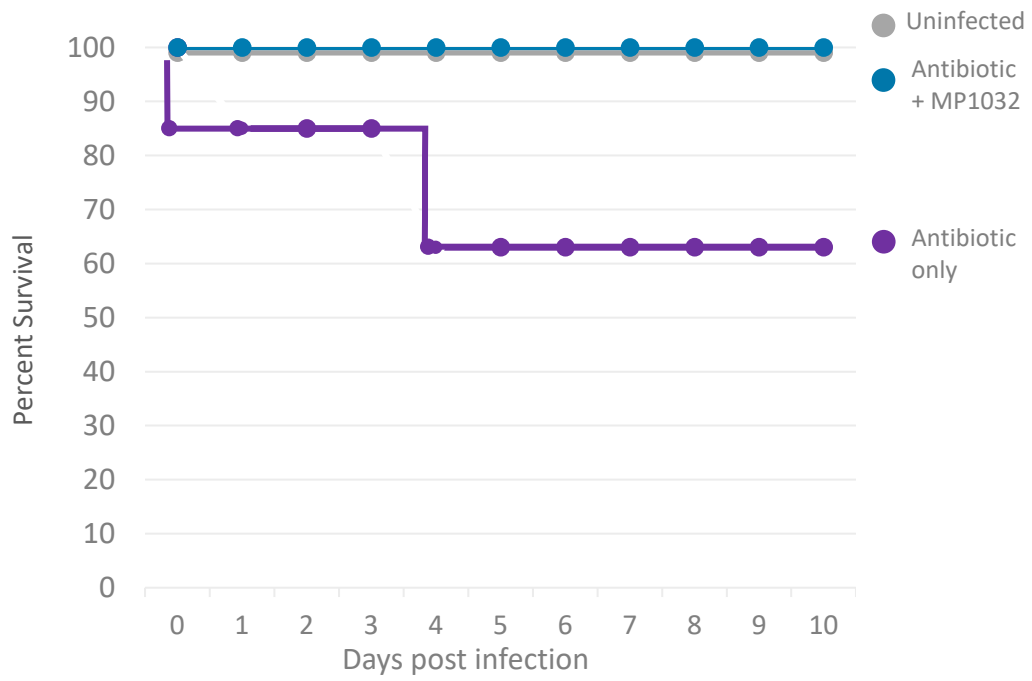
Bacterial Infection
Sepsis

Preclinical POC: Sepsis (1)

Feces-Injection Peritonitis Model (Mouse)

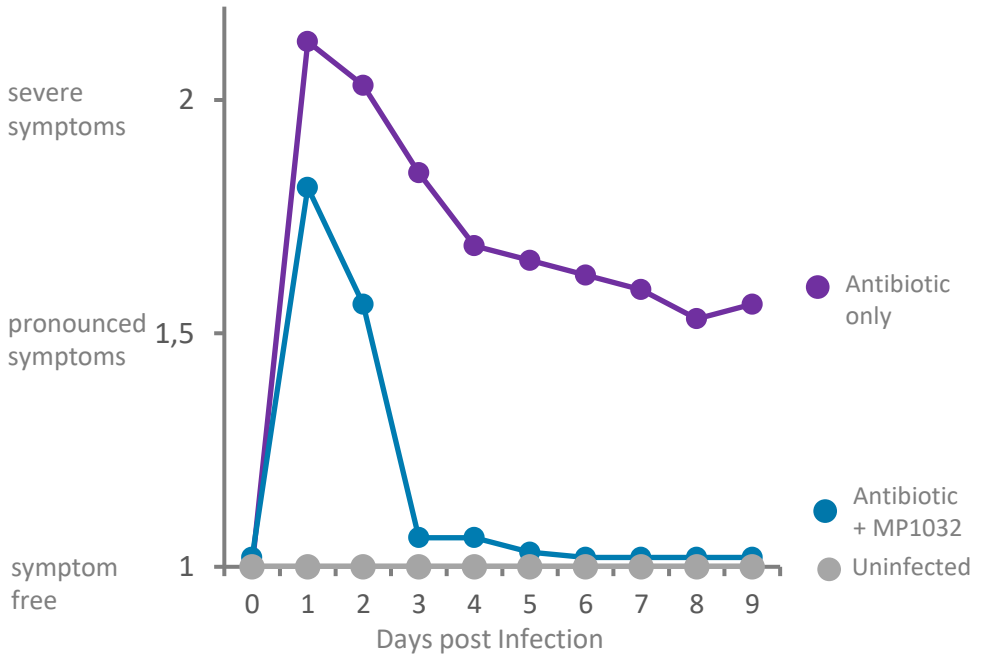
10-Day Survival of Severe Sepsis

Standard Antibiotic treatment vs. Antibiotic + MP1032 combination



Clinical State and Recovery Time

Standard Antibiotic treatment vs. Antibiotic + MP1032 combination



100% animals treated with antibiotic Meropenem plus MP1032 combination therapy survived and fully recovered.
62% of animals in the Meropenem-only group survived, albeit in a clinically poor condition.

The Gonnert score evaluates clinical and behavioral signs of disease and health in animals: movement vs. apathy; food intake, fur, stool. Ranges from 1.0 (normal/healthy) to 3.0 (terminally ill).
Animals treated with antibiotic + MP1032 combination fully recovered within 3 days. Surviving animals treated with antibiotic monotherapy recovered only partially.

Double-blinded study performed by Dr. Ignazio Rubio, Center for Sepsis Control and Care, Jena, Germany

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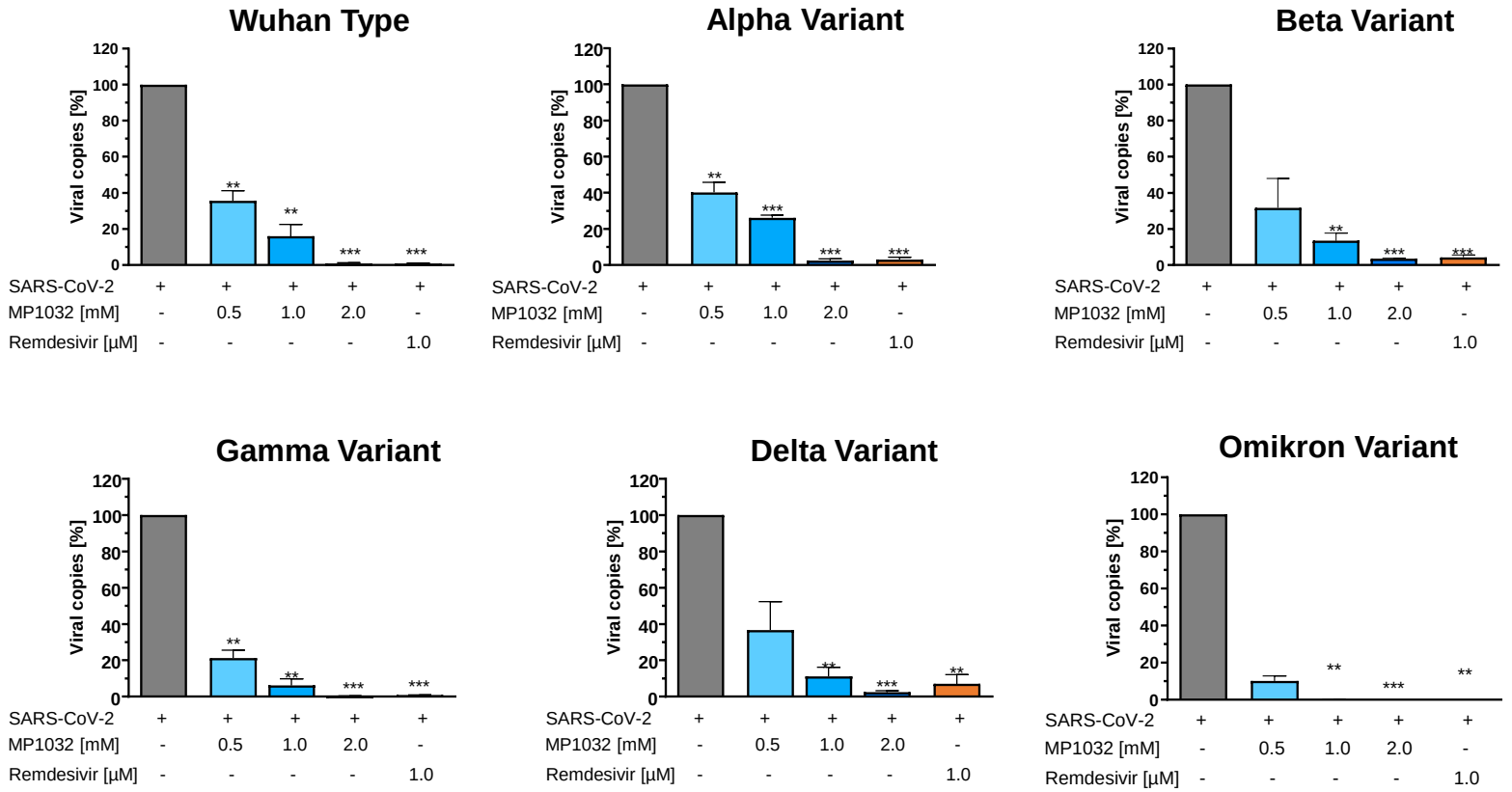
COVID-19

Anti-Viral Activity of MP1032 Against Various SARS-CoV-2 Variants

Host-Directed & Dose Dependent Efficacy - Independent from Virus Variants

MP1032: SARS-CoV-2 Viral Replication in Human Lung Epithelial Cells



Human lung epithelial cells were infected with virus variants of SARS-CoV-2. Virus replication was reproducibly reduced by MP1032 in dose-dependent manner. Anti-viral effect was consistent, independent of virus variant.

Data from Schumann S et al. Immune-Modulating Drug MP1032 with SARS-CoV-2 Antiviral Activity In Vitro: A potential Multi-Target Approach for Prevention and Early Intervention Treatment of COVID-19. Int J Mol Sci. 2020 Nov 20;21(22):8803. Further data from ImmunoLogik GmbH in collaboration with Prof. Ulrich Schubert of University of Erlangen, Germany.

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COVID-19[1] Phase IIa Study Final Data Analysis
PoC for Host-Directed Therapies for Potentially Pandemic Infectious Diseases[1]

Final data analysis reveals significantly better results than early top-line data suggested

Efficacy and safety advantages compared to Standard of Care (SoC)[2]:

- Hospitalization times **reduced by 2.4 days**
  (Better than published data of existing drugs Remdesivir and Molnupiravir at similar endpoints)
- Median Intensive-Care-Unit-stay: **4 days shorter**
- **23% lower** relative long-term (60d) mortality
- **Favorable biomarker** readouts compared to placebo + SoC
  - Lower C-Reactive Protein (CRP) => lower general inflammation
  - Higher GFR => better kidney function (predictor of better clinical outcomes)

[1] Phase IIa study was financed by **EU grant of EUR7.9m**; data were published in ***Lancet Regional Health (Europe);*** this study could serve as PoC for **Host-Directed** Therapies for potentially pandemic infectious diseases such as **COVID, RSV, Influenza** ("**Pandemic Preparedness**")

[2] **Findings from MP1032 treatment group + SoC compared to placebo group + SoC as calculated by Saarmetrics**

USA: Medical Need and Government COVID Therapeutics Strategy

ASPR Administration for Strategic Preparedness & Response

BARDA Biomedical Advanced Research and Development Authority

Outpatient

PrEP	PEP	Therapy
No Illness	Exposed Per CDC Close Contact Criteria	COVID ++ Mild to Moderate Symptoms

Pre-Exposure Prophylaxis (PrEP)

- No approved PrEP treatment available
- „Evusheld“ not authorized for emergency use anymore (FDA)

Post-Exposure Prophylaxis (PEP)

- No current PEP treatments
- Studying new and improved treatments a virus variants change

COVID-19 Treatment

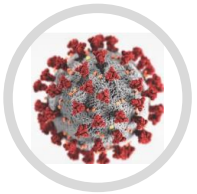
Effective when started within a specific limited timeframe from onset of illness

- Oral antiviral
- IV antiviral
- Monoclonal antibodies (mAbs)

Paxlovid Lagevrio (molnupiravir)

MP1032 COVID Market Opportunity

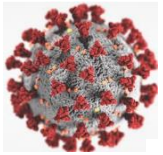
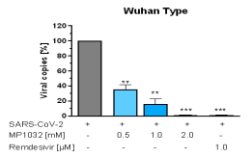
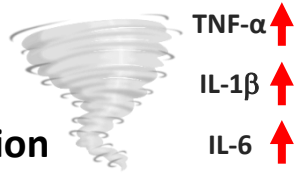
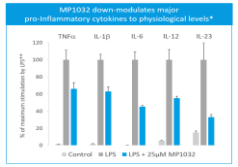
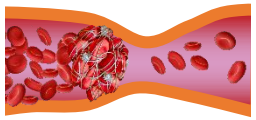
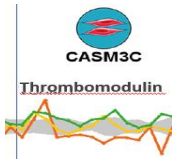
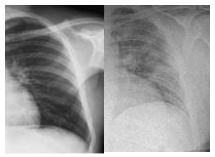
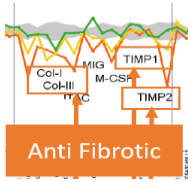
Still no approved drug available for these market segments



MP1032 is Effective Against 4 Cardinal Drivers of Long COVID

MP1032 Immune-Metabolic Modulation: A Multi-modal Therapy Opportunity to Treat Long COVID

COVID-19

Long Covid Pathology	References	MP1032 Therapeutic Effect
1 Persistent Virus 	Couzin-Frankel J. Clues to long COVID. Science. 2022 Jun 17;376(6599):1261-1265 Zollner A, Koch R, et al. Postacute COVID-19 is Characterized by Gut Viral Antigen Persistence in Inflammatory Bowel Diseases. Gastroenterology. 2022 Aug;163(2):495-506	 MP1032 inhibits SARS-CoV-2 replication independent of virus variants **MP1032 Effect** Fights persistent virus
2 Immune Metabolic Dysregulation 	Phetsouphanh C, Darley DR, et al. Immunological dysfunction persists for 8 months following initial mild-to-moderate SARS-CoV-2 infection. Nat Immunol. 2022 Feb;23(2):210-216. Schultheiß C, Willscher E, et al. The IL-1β, IL-6, and TNF cytokine triad is associated with post-acute sequelae of COVID-19. Cell Rep Med. 2022 Jun 21;3(6):100663	 MP1032 inhibits pathologic cytokine release **MP1032 Effect** Normalization of persistent immune dysregulation
3 Micro Emboliams 	Buonsenso D, Di Giuda D, et al. Evidence of lung perfusion defects and ongoing inflammation in an adolescent with post-acute sequelae of SARS-CoV-2 infection. Lancet Child Adolesc Health. 2021 Sep;5(9):677-680.	 MP1032 induces the endogenous factor thrombomodulin **MP1032 Effect** Prevention of micro-embolisms
4 Lung Fibrosis 	Mohammadi A, Balan I, et al. Post-COVID-19 Pulmonary Fibrosis. Cureus. 2022 Mar 2;14(3)	 MP1032 inhibits fibrotic biomarkers **MP1032 Effect** Inhibits pulmonary fibrosis

Long COVID is emerging as a multi-facetted systemic disease which shows the typical hallmarks of pathologic macrophage re-programming. This has detrimental effects on a number of different organ systems. MP1032-mediated macrophage metabolic modulation is a drug mechanism that broadly targets the diverse causes and symptoms of Long Covid. The high unmet medical need and lack of approved therapeutics for Long Covid makes this a highly promising and attractive target indication for MP1032.

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